RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

Vol. 72 APRIL 1959 No. 4

The Radiologist Looks at Radiation Hazards[1]

PAUL C. HODGES, M.D.

WHEN GENETICISTS, biophysicists, and radiologists sit down together for a full-day conference, as they did recently in St. Louis under the sponsorship of the National Research Council (1), they find themselves essentially in agreement about the genetic and other health hazards of ionizing radiations of all sorts and the measures that should be taken to reduce those hazards to a minimum. But prosaic facts may have little reader appeal and unfortunately a few of the people who make their living writing for the popular magazines find it profitable to whoop it up whenever they smell the faintest odor of disagreement.

Certainly the exposure of human tissues to ionizing radiations should be kept as low as is practical. There are many safeguards that can be built into x-ray apparatus and incorporated into x-ray technics to reduce the tissue dose for a particular examination, and certainly it is important to avoid unnecessary examinations.

I shall attempt here to epitomize the clinical implications of the work of the biophysicists and geneticists, who speak for themselves, to weigh as best I can the advantages and risks involved in diagnostic radiology, and to point out what is being done and what further can be done to reduce to a minimum the tissue doses delivered in that procedure.

LEUKEMOGENESIS

Leukemia develops in approximately 6 per 100,000 persons throughout the world each year. It seems unlikely that this normal incidence, which is uniform over the globe, is caused by background radiation, which varies widely from place to place. There is no reason to doubt, however, that larger doses of radiation can produce leukemia, important evidence being its tenfold incidence in radiologists as compared with all other physicians, its incidence in Hiroshima survivors, and an increased occurrence in heavily irradiated laboratory animals. Even in animals, however, to say nothing of man, it remains to be shown that fractional body doses of the magnitude involved in roentgen examination increase the leukemia rate. We are justified merely in saying that, since it is within the realm of possibility that the tissue dose delivered in extensive and repeated roentgen examinations involving *major portions* of the body may *possibly* increase slightly the chance that the patient will develop leukemia, it is well to avoid such studies unless there are sound medical reasons for them.

GENETIC EFFECT

There is good theoretical reason to believe that the increased mutation rate and resulting genetic change observed in heavily

[1] Presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

irradiated fruit flies and mice will occur in man. Without exception, all estimates of the existence, nature, and magnitude of radiation-induced genetic changes are based on inferences from high-level experiments on animals. Human geneticists have begun to study human tissue cultures and the Hiroshima survivors are being submitted to intensive and long-run investigation, but it will be a long time before there is evidence with which to support or refute theory. Meanwhile, since most geneticists believe that increased mutation rates are bad for the race and many are convinced that there is no threshold dose below which the mutation rate remains unaffected, it is obvious that we should do everything in our power to reduce the amount of radiation received by the gonads (2). It is quite possible to keep this dosage low, relative to natural background, in all examinations except those in which the gonads inevitably lie in the direct roentgen beam. I do not argue that unavoidable natural background produces no genetic change nor that its existence justifies the addition of avoidable gonadal doses from diagnostic raying, but, with the exception of those cases in which the gonads inevitably lie in the direct beam, the dose may be kept smaller than the avoidable increases in natural background which all of us accept as reasonable and, for practical purposes, harmless. For example, during the making of a 70-mm. chest microfilm at The University of Chicago, the average adult male receives a testicular dose of 0.05 mr. If this male had been living in a frame house in San Francisco and chose to visit Denver and stay there in a brick hotel for 3.6 days, the increased background from cosmic rays and the radioactivity of stone, brick, and mortar would add a testicular dose of approximately the same amount. If he climbed Pikes Peak and sat for a while on a rock, the dose would be even larger. No one has sponsored or should sponsor legislation requiring all of us to live in tents or frame houses at sea level, and it is not likely that even radiation fanatics believe that boys should be advised, urged, or even required to refrain from scaling Pikes Peak and sitting on a rock to admire the view lest the testicular dose thus acquired jeopardize the future of the race.

SHORTENING OF LIFE SPAN

Experiments with mice have established beyond question the fact that the life span is shortened regularly by heavy irradiation and to a predictable degree. Even for mice, however, experiments with doses as small as those delivered in diagnostic radiology remain to be done, and there are no experiments of any sort in man. These cold, hard facts did not, however, prevent *Time* magazine's science writer from stating (3): "Last week, at the First International Congress of Radiation Research in Burlington, Vermont, Brookhaven National Laboratory's Dr. Howard J. Curtis reported evidence that a single modern fluoroscopic examination of a pregnant woman's pelvis will shorten her child's life by two weeks." This is strong meat that will be devoured and long remembered by the uninitiated, whereas the article in *Science* (4) will be read only by those who already have a pretty good acquaintance with the facts. The latter reads in part: "The shortening of the life span in small rodents exposed to large doses has suggested the possibility that certain degenerative processes may be aggravated by continued exposure to low radiation levels. Such a shortening has also been inferred from an analysis of the published death rates of United States radiologists compared with those of certain other groups of medical men. However, studies in the United Kingdom have failed to demonstrate such an effect. . . . Hence, it is impossible at the present time to estimate with any assurance the effect upon biometrical characters of any given level of irradiation of human populations. Much further research throughout this field is therefore needed. . . . Any present attempt to evaluate the effects of sources of radiation to which the world population is exposed can produce only tentative estimates with wide margins of uncertainty."

Probably Curtis was misquoted. I assume that what he said, in effect, was: "*If* we assume that the curve for the shortening of the life span of mice exposed to heavy irradiation can be extrapolated through zero, thus proving that there is no threshold and that some life shortening will occur for even the smallest doses, and *if* we may assume that the effect in man is the same as in mice, then we might argue that even a dose as small as that delivered to the fetus of a pregnant woman during the course of the roentgen examination of her pelvis would result in shortening the life expectancy of her child from approximately sixty-five years to approximately sixty-four years and fifty weeks."

With the years I have developed a lively respect for the honesty and sagacity of *Time* science writers, and I prefer to believe that the garbling of the Curtis talk may have been done by a rewrite man who, close to press time, did a slipshod job of trimming a rather long story to fit a limited space.

ADVANTAGES *versus* DISADVANTAGES OF DIAGNOSTIC RADIOLOGY

It has not been shown and in my opinion never will be shown that the extremely small tissue doses delivered in properly conducted roentgen examinations increase the mutation rate or the incidence of leukemia, or shorten the life span, but there is every reason to believe that, with larger doses in man, as in laboratory animals, these effects will be produced. Our policy, therefore, as physicians and radiologists, should be to take every practical precaution toward keeping such doses at a minimum, doing what we can to allay hysteria, and seeking always to establish the point that, when there is genuine clinical need for roentgen examination, and when that examination is done by a competent radiologist, the health risk to the patient and his progeny can be kept very small relative to the risk of getting along without the examination.

When one attempts to quantitate advantage *versus* risk in the matter of roentgen tissue doses, he faces almost insuperable difficulties. Mortality tables and computations of operative hazards are available for many diseases and surgical procedures, but quantitative information is lacking as to the radiation risk of altered mutation rate or shortened life and is only suggested, not proved, in the case of leukemogenesis.

Let us consider the latter risk relative to the clinical value of pelvic roentgen examinations of pregnant women. Assuming the soundness of the English work on leukemogenesis in children exposed to diagnostic radiation *in utero* but, for convenience in computation, changing the leukemia rate from 6 per 100,000 to 5 per 100,000, we may argue that pelvic x-ray examinations on 100,000 pregnant women would induce leukemia in 5 children in whom the disease would otherwise not have developed. When a competent obstetrician has decided that a particular pregnancy must be terminated either by cesarean section or by destruction of the fetus and its removal from below, the choice between the two procedures rests largely on the question of the condition of the fetus. In most cases, clinical evidence is adequate to establish the absence of such abnormalities as microcephaly, hydrocephaly, or chondrodystrophy, but when the diagnosis is in doubt roentgen assistance is needed. If, through fear of fetal radiation damage, such examination is withheld, what price is paid in terms of risk of maternal life? In good hospitals throughout the country, the mortality from cesarean section is 0.1 per cent, or 100 deaths in 100,000 sections, so that, in this particular situation, the ratio of the maternal hazard of not conducting a roentgen examination to the fetal risk involved in doing so is 20 to 1. There should be added, also, the saving of some fetal lives where abnormality suggested by the clinical observations is ruled out roentgenographically.

This 20 to 1 ratio is offered tentatively and with full realization of the fact that it may need revision upward or downward because the vital statistics of childbirth are tricky and many factors not immediately

Fig. 1. Testicular shield.

obvious may affect the figures. For example, the 0.1 per cent mortality from cesarean section is a crude estimate which, for my purposes, must be corrected for those cases in which a contracted pelvis is the only indication. On the other hand, the crude statistics provide no measure of the risk to mother and fetus in subsequent pregnancies in cases where a first cesarean operation could have been avoided if x-ray examination had been done. My obstetrical colleagues and I are seeking expert advice in these matters and hope that eventually we may speak on this subject with more confidence than I feel at the moment.

X-ray pelvimetry is not necessary as a routine measure and should not be done but, when a careful and competent clinical work-up indicates its desirability, such examination should be performed with full confidence that the calculated risk is not larger than risks of other sorts that face physicians every day in the practice of medicine. The argument becomes vastly stronger when the examination needed by a pregnant woman does not involve direct exposure of the pregnant uterus.

Fig. 2. Roentgenogram of pelvis with shield in position. Tissue dose to testicle reduced by 95 per cent.

The experienced and conscientious physician will attempt to anticipate or postpone x-ray examinations that are merely convenient but not essential to the well-being of the expectant mother. On the other hand, he will realize that pregnancy increases rather than decreases the desirability of x-ray examinations of the chest, extremities, or even abdomen, if these are essential to the proper guarding of her health or life.

FACTORS FOR MINIMIZING TISSUE DOSE

Among numerous means of keeping tissue doses at a minimum, the following are of particular importance.

(1) Unnecessary examinations should be avoided. It is morally wrong to waste the money of the patient or of society on unnecessary examinations of any sort, and this is particularly true in the case of roentgen examinations. Avoid the thoughtless repetition of gastrointestinal and pelvic examinations. In every instance, think first and examine second.

(2) In particular, avoid fluoroscopy. In the average gastrointestinal examination, consisting of fluoroscopy and films, a total of five minutes of fluoroscopy involves a tissue dose approximately ten times that delivered in the making of sixteen films. Fluoroscopy is convenient in practically any type of roentgen study but essential

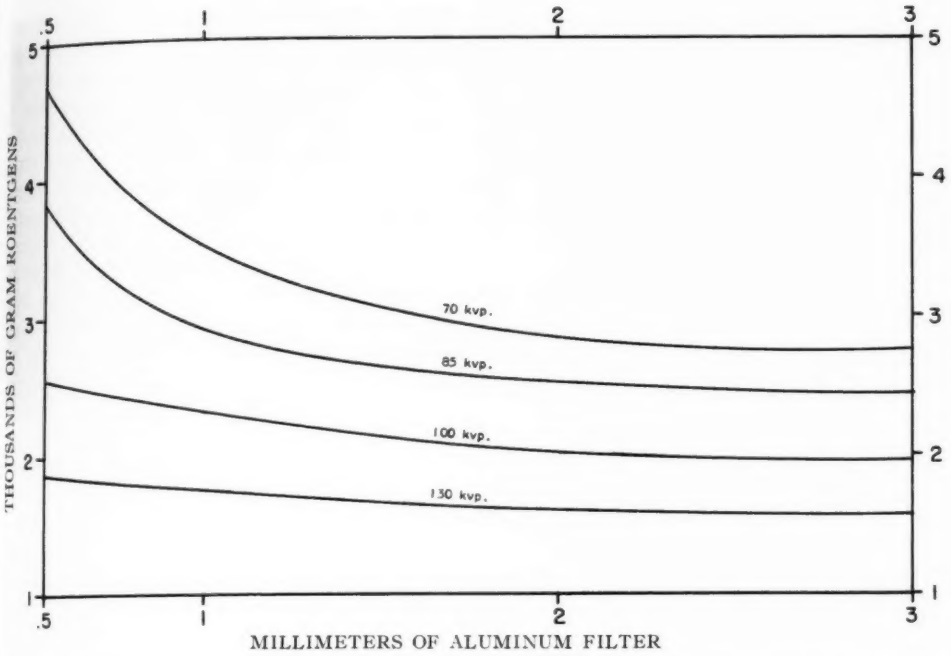

Fig. 3. Saving in tissue dose by raising voltage and increasing thickness of filter. Four curves drawn by Alice McCrea from her computations and extrapolations on Trout's data. Integral dose for 8 × 10-inch field, 20 cm. thick part, to deliver 25 mr transmitted dose to film.

The dose values 1 to 5 on the vertical axis should be looked upon as arbitrary units because of the difficulty in translating one's thinking from doses of approximately 25 mr at the film in terms of thousands of gram roentgens integrated over the entire block of tissue. Increasing filter from 0.5 mm. of aluminum to 2 mm. and increasing voltage from 70 kv to 100 kv drop the tissue dose from approximately 4.75 units to a little over 2 units. An additional millimeter of filter accomplishes almost nothing and increasing the voltage from 100 kv to 130 kv reduces tissue dose by an amount which is not felt to be comparable with the technical disadvantages of 130 kv.

in only a few. Use it only when necessary, never when it is merely a convenience.

(3) In the making of films of the pelvis, the urinary tract, or any other part where the testicle must lie in the direct beam, it should be shielded. It is possible to do this quickly and easily, thereby reducing the testicular dose to approximately 5 per cent of what it would be without the shield (Figs. 1 and 2).

(4) For filming, rather than the more conventional 70 kv. and 0.5-mm. filter, employ a kilovoltage of 90 or 100 and a filter of at least 2 mm., thereby reducing the tissue dose about 50 per cent (5). These factors are adequate; higher voltages and thicker filters lie in the region of diminishing returns (Fig. 3).

(5) Employ fast films and fast screens; give them proper exposure and full development. The slight loss of technical excellence incident to fast film and screen is barely detectable, and the dose can be reduced to about a half. It has been common practice to overexpose films and then underdevelop them by so-called "sight development" in solutions of nonstandard strength and temperature. This produces roentgenograms of reduced quality and may increase the tissue dose by a large factor.

Films are of better quality and the tissue dose falls if, instead of overexposure, just enough exposure is given to allow full development in solutions of standard strength and temperature. Such exposures are best made automatically with phototimers, and processing is best done in automatic devices such as the Eastman X-omat. In spite of their many practical

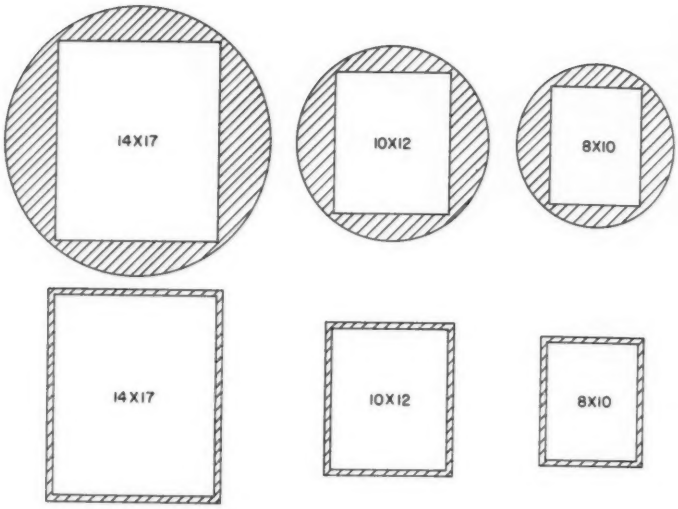

Fig. 4. Reducing tissue dose by small rectangular ports. Clear areas represent radiation striking films of various sizes; cross-hatched areas, radiation striking patient but not film.

In practice, most x-ray work is done either without any circular cones at all or with cones sufficiently large that precise centering of tube and film is not important. The upper half of the figure shows the best possible arrangement when one uses circular ports, an arrangement which in practice almost never obtains. The circular fields cut 1/2 inch beyond the corners of the film.

The lower half of the illustration shows the 1/2-inch belt of waste radiation when rectangular ports are used.

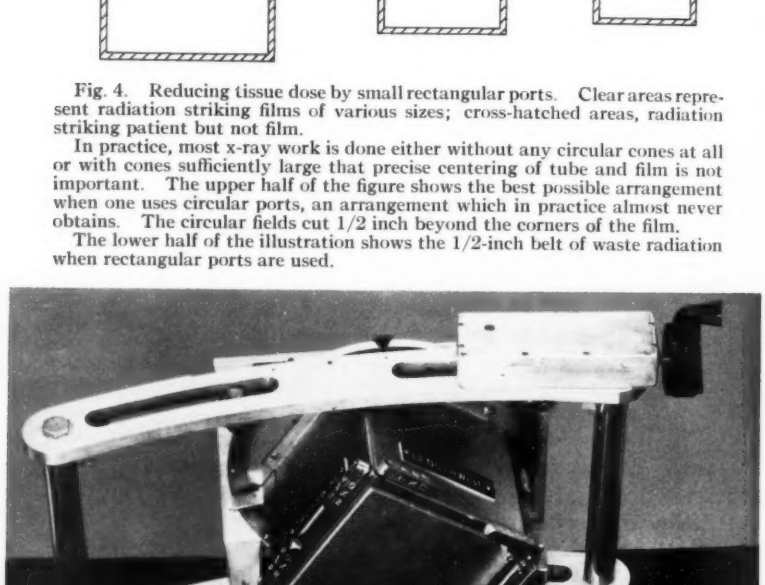

Fig. 5. Detail of rectangular ports. Composite port for 7 × 17-, 8 × 10-, 10 × 12-, and 14 × 17-inch films made at target-film distance of 40 inches. In the illustration the port is rotated halfway between its *longitudinal* and *transverse* positions.

advantages, phototimers have enjoyed little popularity since their introduction more than a decade ago, except in photofluorography. It would be a curious turn of events if now at last they were to be adopted generally as one of the steps in keeping down the radiographic tissue dose.

RECTANGULAR PORTS

Voltage, filtration, film and screen speed, minimum exposure, and full development are important factors in keeping tissue dose at a minimum. There remains the important and frequently neglected matter of restricting the incident beam to

a rectangular cross section barely large enough to include the particular film that is being used.

The port in the ray-proof housing of an x-ray tube is usually circular and the geometry is such that at a target-film distance of 36 inches the base of the conical x-ray beam has a diameter of approximately 25 inches. Usually, but not invariably, an external port or cone is added, and sometimes the technician employs large, medium, and small cones, depending on the size of the film that is being used. Seldom is the diameter of the field of irradiation less than 24 inches for a 14×17-inch film and the field may be equally large or only slightly smaller for films of lesser size. About the best that can be hoped for when the port is circular is a field diameter 1 inch greater than the diagonal of the film. In the case of a 14×17-inch film, this means that, in addition to the exposure required for the roentgenogram, the patient is subjected to an additional 75 per cent of radiation that accomplishes no good whatever. When the film measures 10×12 inches and the radiation disk cuts one-half inch beyond the corners of the film, the useless radiation becomes 80 per cent of the useful beam; for an 8×10-inch film, it becomes 87 per cent. In addition to needlessly irradiating tissue, the unused segments of the beam increase the factor of scattering and thus reduce the quality of the image.

In the case of a 14×17-inch film, a rectangular port that delivers a 15×18-inch rectangle at the plane of the film subjects the patient to only 13.4 per cent of useless radiation. An 11×13-inch rectangle of radiation at the plane of a 10×12-inch film delivers 19.2 per cent of waste radiation; and in the case of an 8×10-inch film, a 9×11-inch rectangle delivers 23.75 per cent of waste radiation (Fig. 4).

The rectangular ports shown in Figure 5 are designed for use with 7×17-inch films lengthwise of the table and for 8×10-inch, 10×12-inch, and 14×17-inch films, either crosswise or lengthwise. In addition, the unit carries a wedge filter that can be brought into the field for such examinations as that of the thoracic spine. With all flaps up, the field extends one-half inch beyond a 14×17-inch film; with the 8×10 flap down, one-half inch beyond an 8×10-inch film, etc. The instrument lacks the universality of commercial adjustable rectangular ports, but in my opinion this is an advantage rather than a disadvantage.

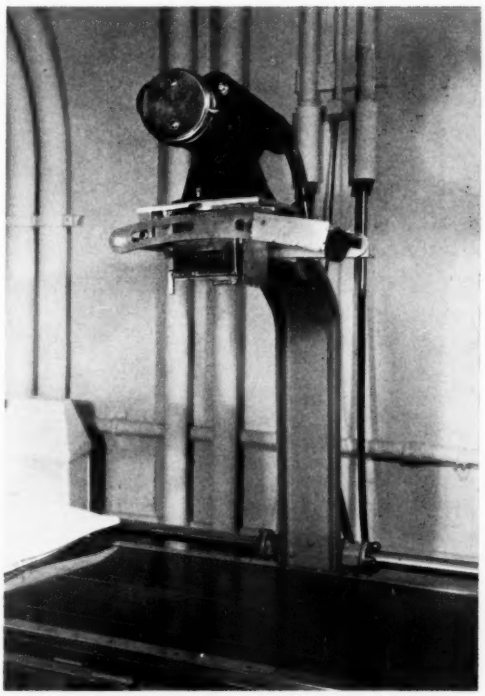

Fig. 6. Rectangular ports assembled on x-ray exposing table. Radiologists and technicians accustomed to commercial equipment in which the position of the x-ray tube in space relative to the film can be adjusted over wide ranges probably will assume, incorrectly, that rigid mounting of the tube is clinically disadvantageous. Those who have worked with rigidly mounted tubes know that they simplify the work in addition to allowing the use of small rectangular ports with consequent sharp reduction in tissue dose.

Figure 6 shows the ports assembled on one of our machines at The University of Chicago, with the 10×12 flap down and the ports oriented lengthwise—*i.e.*, for a film placed with its long axis parallel to the long axis of the table. The tube is rigidly supported with its target 40 inches above the center of the film in the tray of a 16.1 grid. It can be displaced 3 degrees either way from center for stereoscoping without

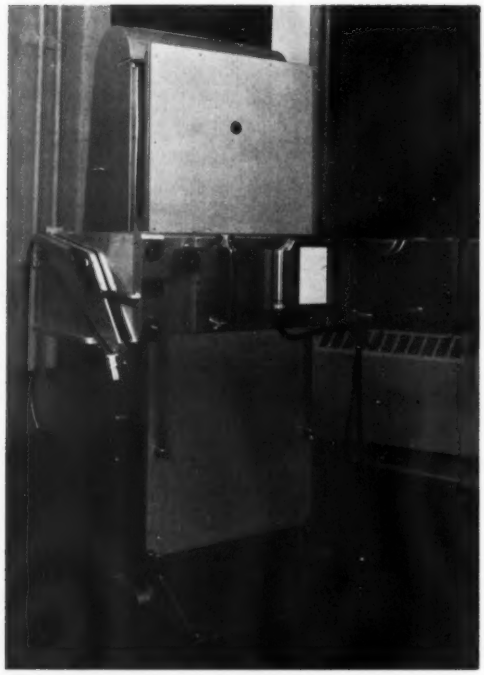

Fig. 7. University of Chicago gastrointestinal filming fluoroscope with 4 1/4 × 7-inch fluoroscopic screen. Small rectangular ports are even more important in fluoroscopy and spot-filming than elsewhere in diagnostic radiology. By standardizing on a small rectangular beam of radiation, mea uring 4 1/4 × 7 inches, it has been possible to simplify the design of the film-changer and greatly decrease tissue dose to patient and operator. Contrary to popular opinion, the smallness of the screen is in no wise disadvantageous.

upsetting alignment between target, rectangular port, and film.

The employment of small rectangular ports is of particular importance in fluoroscopy and spot-filming. Figure 7 shows the present model of a gastrointestinal filming fluoroscope which was first built in our experimental shop many years ago. With the years we have improved the phototimer, film-moving mechanism, and other parts, but have consistently worked with a rectangular beam with a cross section at the film of 4 1/4×7 inches for both fluoroscopy and filming. All types of fluoroscopy are done with the machine and, with experience, the operator finds that the smallness of the field has no clinical disadvantage. On the other hand, it is extremely effective in reducing tissue dose to patient and examiner.

950 East 59th St.
Chicago 37, Ill.

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(For Discussion of this paper, see page 528)

(Pro le summario in interlingua, vider le pagina 531)

The Government Looks at Radiation Hazards[1]

CLINTON C. POWELL, B.S., M.D.[2]

DESPITE THE title of this paper I could hardly presume to speak for the entire Federal Government, much less for our government agencies at all levels—federal, state, and local. Rather, I will confine my remarks to problems of radiation hazards as I see them in the Department of Health, Education, and Welfare.

Increasing public interest and concern, newer scientific information concerning possible deleterious effects of low-level radiation exposure, and rapid expansion of radiation sources have resulted in greater emphasis on radiation hazards within our Department. As examples, within the Public Health Service the activities of the Bureau of State Services have been reorganized by the creation of a new Division of Radiological Health, as outlined by Dr. Russell Morgan in a paper presented at the 1957 meeting of the Radiological Society of North America, and activities of the National Institutes of Health in this area are being expanded within the framework of our broader program in physical biology.

In view of the state of knowledge of those to whom this paper is addressed and the presentations by others in this Symposium, it does not seem necessary to discuss in detail our current fund of information concerning possible radiation effects. I would make one point in this respect, however. I think we all recognize that, in considering possible delayed radiation effects, we are dependent to a large extent upon extrapolations from data on animals, which data are themselves not complete. Thus, differences of opinion continue to exist as to whether or not there is a threshold, particularly for somatic damage; even wider divergences of opinion are current regarding the quantitative significance of low-level radiation exposures.

Radiation exposures of appreciable magnitude, on the other hand, have been an incidental accompaniment to the practice of medicine for several decades. On the basis of this experience, we can place certain upper limits on the damage that might have resulted and still have been unnoticed. However, since many of the effects anticipated are not distinguishable by their nature from disease conditions and abnormalities normally present in the population, such upper limits are sufficiently high that one is hardly justified in assuming a position of complete complacency regarding this problem.

Thus, while discussions concerning the exact quantitative significance of delayed radiation effects will continue, pending more adequate scientific data, the increasing potentialities for radiation exposure of large numbers of people, coupled with the fact that any changes produced might well be undetectable for a period of years after the exposure has occurred, make a conservative attitude defensible. In applying a conservative approach, however, one must consider the damage which can accrue from *lack* of radiation exposure as well as the potential hazards accompanying such exposure. While it would be nice if we could delay many decisions until we have more information, the radiologist in his daily practice, the industrial user of radioisotopes, and those responsible for other potential sources of radiation exposure, face the need of devising practical working premises now, not in the future.

In terms of medical practice, no other individual occupies the favored position of the practitioner of the healing arts in determining whether or not any given exposure is justified in the particular case at hand. Only he can weigh, in the light of best available knowledge, the potential hazards against the probable benefit. I cannot

[1] Presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

[2] Executive Secretary, Radiation Study Section, Division of Research Grants, National Institutes of Health, Public Health Service, U. S. Department of Health, Education, and Welfare.

visualize circumstances under which this right and duty of the practitioner could or should be usurped by another party, such as the government.

There are, however, certain problems which are of necessity within the concern of the government. As an example, I would mention the need for some official control over the installation of such potential radiation hazards as nuclear reactors. I am sure there are few who would advocate complete freedom of activity for any individual who wished to construct a source of this type without regard to its magnitude or potential hazard, to place it in any location he saw fit, and to operate it in any manner he desired. Obviously, some control is indicated, just as we accept some control over other potential hazards in our society, for example, the irresponsible drunken driver.

ASSISTANCE TO THE GOVERNMENT

Government programs will be most meaningful and helpful if they are based on a spirit of mutual assistance and co-operation with appropriate professions. An example of such co-operation is the present relationship between our governmental agencies and the National Committee on Radiation Protection and Measurements—a nongovernmental organization with representation from many professional groups, including the Radiological Society of North America—whose recommendations form the basis for many governmental standards. The quality of such standards is dependent on the scientific knowledge and mature judgment of competent professional individuals. At the same time, the possibility of arbitrary or unwise action on the part of governmental agencies is greatly reduced when such advice and guidance are available.

Governmental health agencies have necessarily developed basic premises and philosophies regarding diagnostic roentgen hazards for use in their own activities, such as tuberculosis case-finding, maternal and child-health and crippled children's programs, as well as for guidance in their approach to broader problems of radiation protection. A general working premise has been developed that the possible hazards of properly conducted x-ray studies are not sufficiently great to deter their use where a significant benefit is anticipated. A corollary is that the potential hazard is sufficiently great to require that all reasonable steps be taken to minimize the radiation exposure to the patient, especially where this can be accomplished with no loss of diagnostic value. It also seems obvious that, in general, the use of proper protective devices and other technics of minimal dose radiography is a much more effective method of reducing total population exposure than a limitation of the number of diagnostic studies. It is my opinion that such a considered operating philosophy has resulted in large part from the high quality of professional consultation available to governmental agencies.

In addition, there appear to be several areas in which sound and well considered government programs can be of assistance to nongovernmental agencies and individuals.

SUPPORT OF RESEARCH

The lack of sufficient quantitative information on low-level radiation hazards has been alluded to before. From experience in my present position, which affords an opportunity to be aware of the support currently provided by the Public Health Service for research outside our own institutions, I believe I can say that a major proportion of radiologists, as well as other scientists, welcome financial support of their research from the government, so long as it is not accompanied by direction or control of their scientific studies. I believe we have demonstrated that it is possible for the government to provide material assistance in a helpful way, without significant interference with scientific freedom.

PUBLIC INFORMATION

As radiologists, we have all been concerned over some of the inflammatory,

scientifically misleading, or inaccurate articles which have appeared in nonscientific publications. To counter these, accurate information must be provided to the general public. The medical profession in general, and the radiologist in particular, are a potent force in this area. At the same time, many a misinformed individual may never reach your offices because of unwarranted fears. Many governmental and voluntary health organizations have had long experience in the problems of lay education on health matters and possess a "know-how" and specialized manpower which can be helpful in the successful prosecution of public education programs.

RADIATION EQUIPMENT USED IN THE HEALING ARTS

Although the detailed accuracy of the available data is subject to question, it seems certain that the employment of radiation in the healing arts currently represents our largest single source of man-made radiation exposure. I would hasten to point out that this use of man-made radiation can also claim to be the one which has proved of the greatest benefit to mankind over the past decades. However, since the potential damage from radiation exposure is independent of its origin, and since governmental agencies have a legitimate concern over certain radiation sources, it is difficult to rationalize an attitude whereby this large use of man-made radiation would be completely ignored by the official agencies. This is not to say, however, that control should be exerted over such sources, especially in the same sense that control is being exercised over such non-beneficial uses of radiation as that of the shoe-fitting fluoroscope.

While decisions as to how and when radiation should be used in the healing arts must remain with the medical practitioner, some evaluation of the magnitude of this exposure is essential in assessing the significance of total radiation exposure from all sources. Several official health agencies already have statutes on the books requiring the registration of all radiation sources within their geographical jurisdictions. In some cases this has been interpreted as tantamount to licensing, which it is not. A registration activity carried on merely to locate sources as a matter of information does not exert any control over the possession or use of such sources, as would a licensing procedure. At the same time, it does not imply any approval of the source, its possession, or its use. Thus, registration of an x-ray machine with a health department does not provide any stated or implied approval. On the other hand, inspection of such a source by either a governmental or nongovernmental group or individual might well provide useful information in the event of medicolegal action.

I think we are all familiar with individual cases in which radiation equipment has been used which delivered doses far in excess of those essential to obtain the desired diagnostic information. An evaluation of the output of equipment, physical adequacy of the shielding, appropriateness of coning, adequacy of filtration, and many similar factors can be accomplished by specially trained individuals without sacrifice of the time of the medical practitioner. It appears entirely possible to me that such surveys of equipment could be accomplished by appropriate government agencies as a service to the medical profession at an overall expense of manpower and funds appreciably less than may be presently required if the practitioner conducts such studies himself. In addition, a determination as to whether or not all reasonable steps have been taken to maintain equipment in a condition to yield the minimal practical dose is one beyond the training of some practitioners of the healing arts. It should be realized that I am referring only to the adequacy of physical safety of the equipment. In my mind, this is quite a different matter from the question as to how the equipment is used. The latter is obviously a professional decision, and only through adequate realization of the problems on the part of those using such equipment can safe operation

be accomplished. I believe that any attempts to control specific clinical technics by legislation or inspection are undesirable and destined to failure. I would point out, however, that in similar circumstances it has been possible for the government to provide assistance welcomed by professional groups, without interfering with their prerogatives. As examples, I would point to present activities of the Food and Drug Administration and the Division of Biologics Standards of the National Institutes of Health in regulating the quality and effectiveness of drugs and biologics.

A related problem is the question of the disposition of obsolete or outmoded equipment. We have seen equipment which a radiologist considered unsatisfactory for his use become diverted to the employment of nonmedical practitioners, for non-medical use, sometimes with an accompanying significant hazard. Governmental agencies might well be in a position to help prevent such diversion of equipment from ethical applications into more hazardous channels. Although the medical and allied professions have been primarily responsible for the establishment of adequate standards of professional practice, every state in this country has licensing laws to protect the public against unethical and untrained individuals who would misrepresent their status and abilities. These laws have become necessary to control those few recalcitrant and conscienceless people who would ignore the sound standards established by the professions. In several jurisdictions, however, the law carefully protects the public from the danger of inadequate diagnoses purveyed by untrained individuals, whether obtained by use of roentgen rays or by other devices, yet does nothing to afford protection against needless and sometimes hazardous radiation exposures at the hands of these same individuals. I think we would agree that this is not a logical situation. I am not advocating that the use of radiation-producing equipment be limited to a single group or groups of individuals on the basis of arbitrary decisions by governmental authorities. I do wish to point out, however, that just as the official agencies are of assistance in enforcing other standards established by the professions in the general practice of the healing arts, they may also be of assistance in enforcing those standards which may be established with your guidance.

SUMMARY

This discussion, I believe, serves to point up that only through mutual co-operation between the individual practitioner, his organizations, and official government agencies, is a reasonable and appropriate approach to the problem of radiation hazards likely. Wholehearted co-operation and active participation of radiologists in the programs of governmental agencies are, I believe, some of the best ways to assure the avoidance of ill advised and ill-considered action.

The government in return can be of help in the support of research programs, in public education, in the maintenance of equipment in the safest operating condition, and in providing a legal basis for exclusion of the untrained and incompetent individual from using a potentially hazardous piece of equipment.

National Institutes of Health
Bethesda, Md.

(*For Discussion of this paper, see page 528*)

(*Pro le summario in interlingua, vider le pagina 493*)

Hazards of Diagnostic Radiology: A Physicist's Point of View[1]

EDWARD W. WEBSTER, Ph.D.

THE PHYSICIST looking at radiation hazards sees a diverse and growing field of activity. This is illustrated by the problem of nuclear power station location, on the one hand, and of manned space flight through newly discovered radiation belts, on the other. For half a century this activity was centered on the problem of protection against x-rays and radium. The mutation which evolved the health physicist occurred in 1942, when the practicability of the nuclear reactor was demonstrated. The enormous potentiality of this device as a radiation source has provided the main impetus for the rapid development of health physics.

In the last few years, another reason for the growth of health physics has appeared. Whereas, even ten years ago, the hazard was considered to be limited to the user of radiant energy, today the whole population is considered at risk. This conceptual change is due largely to the geneticists, who maintain that even the smallest quantity of radiation may produce damaging effects on the human genetic pool. The change has been amplified by other biological effects of low-level radiation, notably carcinogenesis and life-span shortening. This point of view, dramatically publicized by the fallout controversy, is the power behind current legislative action.

The original parent problems of protection against x-rays in medical use have been fundamentally widened by this new concept of hazard, particularly as the patient rather than the practitioner is now the object of interest. The present paper is an attempt to review from the biophysical standpoint possible hazards of diagnostic radiography to the patient and to discuss physical methods for their reduction.

THE PROBLEM

The subject of medical radiation hazards has been treated exhaustively from the point of view of the whole population by various national and international bodies. The physician, however, contemplating the advisability of a particular radiographic examination, must solve his problem on an individual basis. He is adjured "to weigh the risk against the benefit." The physicist approaching this problem follows a well defined path. He is a quantitative person; his inclination is to affix numbers to any phenomenon to describe its size, importance, frequency of occurrence, and general physical properties. He believes that two opposing considerations can best be weighed numerically. It is therefore important to attempt numerical estimates of individual risk in radiodiagnostic examinations. Any numbers quoted in this connection will have a large degree of uncertainty; yet even order of magnitude numbers or pessimistic numbers can be useful.

A constructive evaluation of diagnostic hazards poses the following questions for answer:

1. What is the relationship of dose to hazard for the individual?
2. How much dose and, therefore, how much hazard is involved in a given examination?
3. What is the likely benefit to the individual of a given examination?
4. What can be done to reduce the hazard, that is, the dose?

The first question has subsidiary parts, since hazard is related to the part of the body exposed, the kind of patient exposed (particularly his age), and the technical nature of the exposure (volume exposed, possibly dose rate). The second question is entirely a matter of physical measure-

[1] From the Department of Radiology, Massachusetts General Hospital, Boston, Mass. Based on "The Physicist Looks at Radiation Hazards," presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

ment within prescribed technical parameters. The third question cannot be answered by the physicist: generally only the physician can estimate benefit. The fourth question is also a matter of technology; it has relevance only if a lower dose carries with it a lower hazard, so that overall benefit can be increased.

1. RELATIONSHIP OF DOSE TO HAZARD

In diagnostic radiology we are concerned with exposures of the order of 1 r to limited parts of the body. In this particular context the relationship of dose to hazard is not known. Nevertheless, national and international bodies of scientists (1–4) have been speculating on this problem for the past three years and two main points of view seem to have emerged—the optimistic and the pessimistic.

The *optimistic* view holds that at levels of 1 r there is no hazard to an exposed individual *per se*. This conclusion expresses belief in a threshold for nonreparable biologic damage. Austin Brues (5) has recently examined with favor the impressive evidence that carcinogenesis by any agent, including radiation, has a much lower (possibly zero) probability at low doses than at higher doses. Even the optimists concede a genetic hazard to the offspring, but it may be considerably less than that based on extrapolation from mouse data, at much higher doses.

The *pessimistic* view is that at levels of 1 r there is a definite probability of permanent damage in terms of delayed effects on the individual, which can be extrapolated from observations at much higher dose levels. This conclusion applies even more strongly to genetic damage.

It is instructive to estimate the probabilities of both somatic and genetic damage if the pessimists are right. Three kinds of somatic damage to a radiodiagnostically exposed individual are considered.

Leukemia: A recent authoritative discussion of leukemia in relation to irradiation is included in the Report of the United Nations Scientific Committee on the Effects of Atomic Radiation (4). An extrapolation of the analysis of Court-Brown and Doll (6) of ankylosing spondylitis cases in which leukemia developed after therapeutic spinal irradiation leads to an estimate of 1.5 cases of leukemia per million per year after a mean dose of 1 rad to the whole active bone marrow. Making the further assumption of fifteen subsequent years at risk, the Report estimates a total probability of 20 cases per million per rad.

Carcinogenesis Other Than Leukemia: The basis for pessimistic human estimates of radiation carcinogenesis exclusive of leukemia is even more tenuous. However, since we are seeking only an order of magnitude number, it is proposed to consider the data of Simpson and Hempelmann (7) and of the Stewart study (8). These two studies tend to show, in the words of Sir MacFarlane Burnet (9), that "the increase of leukemia resulting from irradiation is almost exactly the same as the total of malignant tumors from all other types of cell that could be ascribed to radiation."

In the first of these studies, relating to therapeutic irradiation of the thymus gland in infants, the number of cases of malignant disease other than leukemia which were found on follow-up was about equal to the number of leukemia cases. To be most pessimistic, we assume a linear relation between cancer incidence and radiation dose. We hypothesize further that the average bone-marrow dose is the critical factor for leukemia induction, while average whole-body dose is the important parameter for induction of other cancer. It may then be deduced, in the case of 14 × 17-inch exposures in adults, that cancer incidence per rad of midplane dose in the exposed region is about one-half of the leukemia incidence per rad of mean marrow dose (see Appendix). From the study of Stewart *et al.* it may be concluded that the incidence of cancer, other than leukemia, in children bears approximately the same relationship to previous maternal irradiation during

pregnancy as does the leukemia incidence. Since the mean tissue dose in the fetus (midplane) will be essentially the same as the bone-marrow dose, it follows that the incidence of cancer after irradiation may be the same per rad to the midplane as the incidence of leukemia per rad of mean marrow dose. These two estimates of cancer incidence differ by a factor of two. Since, however, we are concerned with partial-body irradiation of adults, rather than with whole-body irradiation of fetuses, it is preferable to take the figure derived from the thymus irradiation study in infants. Thus we assume, pessimistically, that the possible total cancer cases other than leukemia are 10 per million per rad to the midplane for large field examinations.

This number is not incompatible with the fact that a significant increase in cancer incidence has not been observed in exposed adult populations where a significant increase in leukemia has been observed, *e.g.*, in the Japanese A-bomb survivors. Since the normal cancer incidence is much higher than that of leukemia (in the United States the rate is forty times higher), a small increase in the number of cancer cases would be insignificant while an increase in leukemia cases by the same number would be obvious.

Life Span Shortening: The author is inclined to dismiss the hazard of a shortened life span, even in the context of pessimism, for the following reasons. Recent studies have failed to disclose any significant life span shortening in radiologists in either the United States or the United Kingdom (10, 11). Moreover, there is real uncertainty that the life span in animals is shortened by whole-body exposure to low chronic dose rates. In fact, some prolongation of life has been observed (12, 13). Finally, information on partial-body exposure (14) indicates that no significant shortening occurs even for very large doses (700 r) to the entire chest of female mice.

Genetic Effects: Probably the most discussed of the radiation hazards is the genetic effect; yet there is very little *human* data on which to base an estimate of radiomutability. The direct data relate to observed changes in the sex ratio after massive irradiation of the parental gonads. This has been admirably reviewed by Schull and Neel (15). It is possibly significant that the only study of human sex ratio which relates to chronic low-level exposure (in American radiologists) shows a change in ratio contrary to that expected from current genetic theory (15, 16). The widely quoted estimate of 50 r as the dose to double the spontaneous mutation rate in man stems largely from investigations of male mice exposed to large acute doses of 600 r (1–4). Very recent investigations have suggested a less pessimistic situation. There is evidence that the mouse mutation rate under heavy but protracted radiation exposure is considerably less than that for acute exposure. Thus, Carter (17) has estimated 95 r as the doubling dose in mice under chronic gamma irradiation compared with 36 r for acute irradiation, and Russell, Russell, and Kelly (18) have observed a mutation rate four times less in mice irradiated chronically with gamma rays in comparison with that produced by 600 r of acute x-irradiation.

It has been estimated as a most probable statistic by six geneticists on the National Academy of Sciences Committee on Genetic Effects of Atomic Radiation (1) that the probability of a child carrying a new mutation as the result of 1 r exposure to both parents is 0.5 per cent (1 in 200). Hence the probability of inducing mutation in an individual exposure to 1 r would be 1 in 400. This figure is derived from the observed average mutation probability in mice of 25×10^{-8} per locus per roentgen (acute dose) and the assumption of 10,000 loci in man. This estimate of a radiation-induced mutation rate in man is the central value of a range estimated from 10 times lower to 10 times higher. The highest probability implies that all spontaneous mutation is produced by background radiation; this possibility is

TABLE I: ESTIMATED PERSONAL RISKS TO SUBJECT OF EXAMINATION: OPTIMISTIC (THRESHOLD) *versus* PESSIMISTIC (NO THRESHOLD)

Examination	Views	Total Skin Dose	Mid-plane Tissue Dose	Mean* Marrow Dose	Chance of Leukemia		Chance of Other Cancer	
					Thresh.	No Thresh.†	Thresh.	No Thresh.†
		r	r	r				
Pelvis	A-P	0.65	0.15	0.02	zero	1 in 2,500,000	zero	1 in 660,000
Lumbar spine	A-P, lat., spot	8.0	1.0	0.4	zero	1 in 125,000	zero	1 in 100,000
Intravenous pyelography	4 A-P	2.4	0.48	0.16	zero	1 in 300,000	zero	1 in 200,000
Abdomen	A-P	0.6	0.12	0.05	zero	1 in 1,000,000	zero	1 in 800,000
Barium enema	2 P-A	1.8	0.36	0.35	zero	1 in 140,000	zero	1 in 280,000
Upper gastrointestinal	2 P-A	1.8	0.36	0.25	zero	1 in 200,000	zero	1 in 280,000
Hip	A-P, lat.	3.0	0.6	0.03	zero	1 in 1,600,000	zero	1 in 168,000
Lower femur	A-P, lat.	1.0	0.2	0.02	zero	1 in 2,500,000	zero	1 in 500,000
Chest								
14 × 17-inch film	P-A, lat.	0.12	0.02	0.04	zero	1 in 1,200,000	zero	1 in 5,000,000
Microfilm	P-A	0.5	0.1	0.1	zero	1 in 500,000	zero	1 in 1,000,000
Skull	7 exposures	3.8	0.8	0.1	zero	1 in 500,000	zero	1 in 126,000

* Based on U.N. Report (4). † Also assumes linear relation.

dismissed as too remote even for a pessimistic assessment (2, paragraph 178). Therefore, bearing in mind that chronic irradiation is less mutagenic than acute irradiation, we have taken as the pessimistic probability of producing a mutation through diagnostic radiology the above central value, *viz.*, 1 in 400 per roentgen per individual.

The effect of genetic damage in an exposed population which it is convenient from a numerical standpoint to assume is that propounded by Muller (3) and considered in the Statement on Radioactive Fallout by the Advisory Committee on Biology and Medicine of the Atomic Energy Commission (19). This concept is that any mutation, no matter how mildly deleterious, can be considered as a "genetic death," since the milder handicaps will affect more generations of people before extinction through the operation of natural selection and will therefore be just as damaging as a serious mutation of much shorter life. Hence it is proposed to consider any mutation produced as a loss of seventy man-years to future society.

2A. DOSES INVOLVED IN RADIODIAGNOSTIC PROCEDURES

In order to attempt a quantitation of the hazards involved within the limits of the above pessimistic assumptions, it is first necessary to know the dose delivered to the subject in radiodiagnostic examinations. Clearly, several kinds of dose information are required. For an estimate of the leukemia hazard, the mean bone-marrow dose per examination is needed. To calculate the chance of inducing other cancer, the midplane tissue dose must be known. For an assessment of the genetic hazard, the gonad dose is required for both males and females.

The mean bone-marrow dose has been estimated for typical radiographic examinations in the United States by the United Nations Committee (4). These figures are based largely on measurements of skin dose by Webster and Merrill (20). A round estimate of the midplane tissue dose to skull and trunk of the body is 20 per cent of the skin dose. This is based on the 10-cm. depth dose, for large fields, of diagnostic quality radiation at 70 kvp with 2 mm. Al filtration added.

TABLE II: ESTIMATED TOTAL RISK TO DESCENDANTS PER EXAMINATION*

Examination	Views	Gonad Dose		Chance of Producing One Mutation†	
		Male	Female	Male	Female
		r	r		
Pelvis					
Scrotum unprotected	A-P	0.43	0.115	1 in 930	1 in 3,500
Scrotum protected		0.03	0.115	1 in 13,300	1 in 3,500
Lumbar spine	A-P, lat., spot	0.06	0.44	1 in 6,700	1 in 900
Intravenous pyelography	4 A-P	0.05	0.5	1 in 8,000	1 in 800
Abdomen	A-P	0.012	0.125	1 in 33,000	1 in 3,200
Barium enema	2 P-A	0.07	0.44	1 in 5,700	1 in 900
Upper gastrointestinal	2 P-A	0.008	0.120	1 in 50,000	1 in 3,300
Hip	A-P, lat.				
Scrotum unprotected		2.53	0.525	1 in 160	1 in 760
Scrotum protected		0.06	0.525	1 in 6,700	1 in 760
Lower femur	A-P, lat.				
Scrotum unprotected		0.56	0.045	1 in 720	1 in 8,900
Scrotum protected		0.06	0.045	1 in 6,700	1 in 8,900
Chest					
14 × 17-inch film	P-A, lat.	0.00016	0.0008	1 in 2,400,000	1 in 500,000
Microfilm	P-A	0.001‡	0.003‡	1 in 400,000	1 in 130,000
Skull	7 exposures	0.00012	0.0001	1 in 3,300,000	1 in 4,000,000

* This table can be applied only to those individuals who have a definite likelihood of procreating.

† This column gives the central value of a range of probability extending from 10 times smaller to 10 times greater. See text.

‡ These data taken from U.N. Report (4) for the United States. All other gonad dose figures from Webster and Merrill (20).

Finally, the gonad dose may be evaluated from the many measurements recently reported on this subject. For consistency, however, the values recorded by the above authors (20), which would be compatible with the skin and bone-marrow doses, have been utilized for most of the examinations considered.

2B. POSSIBLE HAZARDS IN RADIOGRAPHIC EXAMINATIONS

For these preliminary estimates based on pessimistic assumptions, only the radiographic examinations which are frequent or involve large doses have been considered. The two kinds of hazard have been listed separately in Tables I and II, since they are conceptually different. The first table applies to possible long-term somatic damage in the examinee, whereas the second table applies to possible mutations which may appear in subsequent generations and which in their totality may be regarded as "genetic death." It should be remembered, also, that the possibilities of genetic damage apply only to individuals who will actually procreate in the future. In order to emphasize that there will be no somatic damage if there is an appreciable threshold level of radiation for these effects (*e.g.*, 100 r), this optimistic assessment of risk has also been entered in Table I.

The important conclusion that emerges from these considerations is the extremely low level of personal risk that attends all radiographic examinations. Even the highest exposure (a 3-film examination of the lumbar spine) would appear to carry a *maximum* risk of leukemia of 1 in 125,000 and of other cancer of 1 in 100,000. The risk of genetic damage is also small, but it is considerably larger in many examinations than the personal risk. Those examinations carrying the largest genetic risk will be seen to be those in the male, where the testicles may be directly exposed (*e.g.*, hip, 2 films, 1 in 160). Fortunately, these are the examinations where protection is readily provided. With testicular protection, the maximum male risk drops to very low levels (1 in 10,000). The maximum female mutational risk is of the order of 1 in 1,000. With some common examinations such as those of the chest and skull, the pessimistic risk estimate falls to the order of 1 in a million for a mutation.

Relative Genetic Risks: The environment, of course, produces radiation ex-

TABLE III: DIAGNOSTIC RADIOLOGY *versus* RADIUM WRIST WATCHES

Radiographic Examination	Male Gonad Dose (mr)	Number of Examinations to Equal Dose from Radium Wrist Watch in 10 years*
Pelvis		
Scrotum unprotected	430	0.5
Scrotum protected	30	7
Lumbar spine	60	3
Intravenous pyelography	50	4
Abdomen	12	17
Barium enema	70	3
Upper gastrointestinal	8	25
Hip		
Scrotum unprotected	2,530	0.08
Scrotum protected	60	3
Lower femur		
Scrotum unprotected	560	0.35
Scrotum protected	60	3
Chest		
14 × 17-inch film	0.16	1,200
Microfilm	1	200
Skull	0.12	1,600

* 200 mr as conservative estimate.

posures other than those in radiodiagnostic examinations. Using exactly the same assumptions as above, an interesting comparison of individual genetic risks becomes possible.

(*a*) *Radium-Dial Wrist Watches:* The first comparison is with the wearing of a typical radium-dial wrist watch. Several investigators have measured doses near such watches. Libby (21) quotes 1 μc as being perhaps slightly larger than the average amount of radium. Haybittle (22) quotes a mean radium content (of some watches in England) as 0.25 μc. Chase and Osol (23), measuring the radiation dose rate at 1 inch from the face of 20 watches, estimated the mean as 2.7 mr/hr. The calculated dose to the gonads *per annum*, on the assumption of 12 inches distance from a watch worn continuously, is 80 mr, 20 mr, and 160 mr, respectively, on the basis of these three reports. Since some measurements by the author favor the lowest figure, 20 mr *per annum* will be taken as a conservative estimate.

Table III is derived from the gonad dose data of Table II and expresses the number of radiographic examinations of the principal kinds that an individual may accept before the gonad dose (genetic hazard) equals that received from the average radium-dial wrist watch worn for ten years. Clearly, if the testicles are protected from direct exposure in examinations of a few kinds, several such examinations may be given before the hazard exceeds that of wearing the watch; more than 1,000 chest or skull examinations may be given.

TABLE IV: DIAGNOSTIC RADIOGRAPHY *versus* WEARING TROUSERS

Examination	Male Gonad Dose	Number of Examinations for Same Genetic Effect as Wearing Trousers*
	r	
Pelvis		
Scrotum unprotected	0.43	90
Scrotum protected	0.03	1,200
Lumbar spine	0.06	700
Intravenous pyelography	0.05	800
Abdomen	0.012	3,000
Barium enema study	0.070	600
Upper gastrointestinal series	0.008	5,000
Hip		
Scrotum unprotected	2.53	16
Scrotum protected	0.06	700
Lower femur		
Scrotum unprotected	0.56	70
Scrotum protected	0.06	700
Chest		
14 × 17-inch film	0.00016	250,000
Microfilm	0.001	40,000
Skull	0.00012	300,000

* Assumed as 40 r equivalent.

(*b*) *Wearing Trousers:* It is possible to estimate, although on much less certain grounds, the dose of radiation to the gonads which is equivalent to the male habit of wearing trousers throughout the genetically effective life span. Ehrenberg, von Ehrenstein, and Hedgran (24) reported recently on their studies of the increased gonad temperature in the male due to normal clothing. The observed increase was 3.3° C. Assuming that the temperature dependence of spontaneous

TABLE V: MEASURED DATA FOR PHOTOFLUOROGRAPHIC CHEST SURVEY UNITS

kvp	mas	Added Filter	Target–Screen Distance	Unit Type	Skin Dose	Gonad Dose Male	Gonad Dose Female	Reference
					r	mr	mr	
83	24		36 in.	lens		0.25	0.15	Stanford and Vance (44)
80		2.0 mm. Al		lens		0.47	4.7	Hodges (26)
80		2.0 mm. Al		mirror		0.1	1.0	Hodges (26)
						6.7	3.0	Norwood (45)
						0.25	0.15	Hammer-Jacobsen (4)
						1	2	U.N.: Austria (4)
						0.3	0.3	U.N.: France (4)
85	16		75 cm.	mirror		0.21	0.5	Larsson (51)
						1	3	Billings *et al.* (46)
					0.87	0.73	15	Feldman *et al.* (48)
100	45	1.0 mm. Al	40 in.	lens	1.2	2	10	Webster and Merrill (20)
		0.5 mm. Al			0.7	...	...	Handloser and Love (49)
					1.2			
				mirror		0.11	...	Koren and Maudal (47)
90	30	2.4 mm. Al		lens	0.52	2	1	Laughlin *et al.* (25)

Mean of higher readings (lens?): male 1.7 mr; female 5 mr
Mean of lower readings (mirror?): male 0.2 mr; female 0.4 mr

mutation in man is the same as that observed in the fruit fly, these authors calculate that 85 per cent of spontaneous mutation in the male would be due to the temperature rise. This is estimated as equivalent to a radiation dose of about 40 r. Table IV lists the number of radiographic examinations necessary to yield such a radiation dose.

The point of these comparisons is to show that there are activities of our society apparently accepted with equanimity which may produce noxious effects in the individual of a magnitude similar to those attributed to medical radiation; yet these activities may contribute less to our well-being and hence are deserving of an investigation equally as searching as that currently being given to diagnostic radiology.

3. BENEFIT *versus* HAZARD

The author, as a physicist, is not competent to discuss the benefit to the individual of radiodiagnostic examinations. A useful general conclusion emerges, however, from the estimates of maximum risk (Tables I and II): that the hazards, even at worst, are very small and are mainly to posterity; and that, although the physician must envisage some advantage, it could be relatively minor and certainly does not have to be of life-saving proportions.

The weighing of benefit *versus* hazard on a numerical basis would seem to be almost impossible. Yet in one special case it is felt that this could usefully be done. This is in the field of mass chest surveys; the numerical approach which could be used is outlined below. It is emphasized that, although the numbers quoted are derived from observation, there are yet insufficient data available to make a comparison of benefit and hazard on more than an order-of-magnitude basis.

Benefit versus Hazard in Mass Chest Surveys: (a) Hazard (Social Cost): In order to evaluate hazard according to our previous discussion, it is necessary to establish average figures for radiation exposure to skin, bone marrow, and gonads in mass chest surveys. The data, particularly on gonad dose, cover a wide range; typical measurements are shown in Table V. Several ranges of exposure are possible, depending on the type of photofluorographic unit used and the attention paid to its filtration and collimation. Four kinds of system have been selected as follows: (*A*) a well collimated mirror-optics unit; (*B*) a well collimated lens-optics unit; (*C*) a poorly collimated, poorly filtered lens-optics unit; and, solely for comparison, (*D*) a well collimated 14 × 17-inch standard chest installation. Typical doses for these systems are indicated in Table VI.

TABLE VI: EXPOSURE DATA FOR THREE KINDS OF MASS MINIATURE RADIOGRAPHY AND 14 × 17-INCH CHEST RADIOGRAPHY

System	Description	Skin	Midplane	Mean Bone Marrow Dose	Gonad Dose Male	Gonad Dose Female	Mean Gonad Dose
		r	r	r	mr	mr	mr
A	Well collimated and filtered, mirror optics, miniature	0.12	0.03	0.024	0.25	0.75	0.5
B	Well collimated and filtered, lens optics, miniature	0.5	0.12	0.1	1	3	2
C	Poorly collimated and filtered, lens optics, miniature	1.0	0.2	0.4	40	200	120
D	Well collimated and filtered, 14 × 17-inch conventional	0.02	0.005	0.004	0.06	0.2	0.13

TABLE VII: PESSIMISTIC HAZARD DUE TO MASS CHEST SURVEYS (20,000,000 FILMS PER ANNUM)

System	Maximum Personal Damage			Future Damage		Total
	Leukemia Total Cases	Other Cancer Total Cases	Man-Years Lost	No. of Mutations	Man-years Lost	Man-years Lost
Miniature A	10	12	500	8	560	1,100
Miniature B	40	48	2,200	32	2,240	4,400
Miniature C	160	80	6,000	1,920	134,000	140,000
14 × 17-inch film	1.6	2	90	2	140	230

The mean bone-marrow dose has been taken as 20 per cent of skin dose for the well collimated systems (25) and as 40 per cent for the poorly collimated system. From analysis of Table V, it is concluded that the gonad dose has a ratio of 3:1 between female and male; a mirror-optics system is assumed to produce four times less dose than a lens system (25, 26). For a poorly filtered and poorly collimated lens system the ovary dose is taken as 20 per cent of the skin dose (10-cm. per cent depth dose) and the testicular dose as 40 mr, the exit dose observed for a lens system by Laughlin *et al.* (25). The 14 × 17-inch data are based on skin and gonad dose measurements by the author (20).

The personal damage possible with 20 million photofluorograms *per annum* is shown in Table VII. It is assumed that one-third of the population surveyed are under age thirty (27). Seventy future man-years are considered lost per mutation and 25 man-years lost per case of malignant disease. The main conclusion of this analysis is that a small amount of damage is done (on pessimistic assumptions) with well collimated equipment, but there is an inordinately high genetic risk if the gonads are in the useful beam because of poor collimation.

(*b*) *Benefit:* The U. S. Public Health Service has attempted in the past to show, by the follow-up of tuberculosis and other cases disclosed by mass chest survey, that there is indeed benefit to the person whose disease is discovered as compared to the one with undiscovered disease. It is obviously difficult to find comparable populations for such an assessment. Recently, however, the Public Health Service published a study by Enterline and Kordan (28) comparing the relative death rate in two equivalent population groups: one of these had been suspected of tuberculosis or heart disease as a result of a survey and had been subject to medical care, while the other was equally suspect on a retrospective second reading of the miniature films made some years later but had, in the interim, received no medical care. The age-race-sex-corrected death rate in the group of "discovered" suspects was one-third less over a period of three and a half years than the death

TABLE VIII: COMPARISON OF BENEFIT AND COST IN MASS CHEST SURVEYS

Benefit		Cost				
		System→	A	B	C	D
Disease suspected	Tuberculosis	Man-yrs. lost in this generation	550	2,200	6,000	90
Number of annual suspects	300,000					
Increased life-span	0.5 year					
Man-years gained	150,000					
		Man-yrs. lost in future	560	2,240	134,000	140
		Total man-yrs. lost	1,100	4,400	140,000	230

rate in the "undiscovered" group, a difference statistically significant at the 5 per cent level ($p = 0.027$). It is important to point out that the fall in death rate in the followed group was due not to a lower mortality from tuberculosis, but was the result of a pronounced reduction in cardiovascular deaths. This Enterline and Kordan attribute to the medical follow-up received by the recognized suspects. Deaths from tuberculosis were too few for any conclusions regarding relative mortality rates from that cause.

For use in the following comparison of benefit and cost, the above data must be expressed in terms of increased life expectancy for the "discovered" suspects. An increase in survival is a corollary of the reduced death rate. At the present time, over the three-and-one-half-year period of the study, an increase of 0.03 year in the mean life span of the "discovered" suspects is deduced. If one assumes that this reduced death rate is maintained for fifteen years, the difference in mean survival time of "discovered" and "undiscovered" groups increases to about six months. For this extrapolation the same rate of increase of death rate with age was assumed for both groups, on the basis of the current U. S. Life Table. It is therefore proposed to use the figure of six months increased life-span for tuberculosis suspects as the benefit to be offset against the losses due to radiation damage. This assessment does not include the statistically less certain benefit to "discovered" cardiac suspects (28). In the absence of information concerning benefit to suspects with chest neoplasms, but with knowledge of the poor five-year survival of treated cases of bronchogenic carcinoma, it is proposed to neglect any benefit from this particular yield.

Annual chest surveys in the United States in recent years have involved about 20 million miniature films and have resulted in the discovery of about one-third of the new active cases of tuberculosis, *i.e.*, about 20,000. On the basis of 1 suspect per 60 films (27–30) or 16 suspects to 1 proved active case, a national number of tuberculosis *suspects* would be 300,000 *per annum*. Hence the benefit *per annum* of national mass chest surveys might be assessed numerically at $300{,}000 \times 0.5$ man-years, or 150,000 man-years (Table VIII).

(*c*) *Conclusion:* For systems *A*, *B*, and *D* it would appear that mass chest surveys show an overwhelming surplus of benefit over cost. Even if the genetic risk is increased ten times in order to give the worst possible hazard (corresponding to a doubling dose equal to background radiation), the benefit is still much greater than the cost. It is also apparent that the minimum risk is afforded by 14×17-inch films. It is obvious, however, that system *C* produces a complete canceling of the benefits. This points up semiquantitatively the great importance of adequately coned and filtered chest-survey units.

The comparison in Table VIII leans heavily on the postulation of a six-month increase in life expectancy for every tuberculosis suspect found by survey. A more valid conclusion is that, with system *B* (the usual one), it is necessary to demonstrate only an average life-span gain of five days per suspect to show a net gain of benefit over pessimistic cost. Enterline's study has already demonstrated a ten-day gain over the short term.

The above analysis is presented largely to illustrate a method of evaluating the advisability of roentgen examinations. Nevertheless, it is apparent that it may be unjustifiable to abandon properly conducted mass chest surveys *solely* on the grounds of excessive hazard. Clearly, further and longer-term studies of comparative survival are indicated to substantiate the tentative conclusions of the single study discussed above.

4. REDUCTION OF DIAGNOSTIC EXPOSURE

The previous discussion illuminates the two forces controlling the current drive toward dose reduction—the desire to make any medical procedure as little hazardous to the patient as possible and the general obligation to future society to minimize as far as possible the addition of further mutations to the genetic pool.

The physicist assumes that no radiological examination is given without a reasonable expectation that information of value to the patient will result. In the face of desirability of an examination, what can be done technically to reduce the dose? The physicist, as distinct from the technician, is inclined to examine the confining limits within which dose reduction can occur; in other words, to answer the question: What sets the limits for dose reduction?

The parameter which typifies patient exposure is the skin dose; that is, if skin dose for a given field size is reduced, then dose everywhere else is reduced. More precisely, on the assumption that a given film or screen dose is necessary, how low can the ratio of skin to film (screen) dose be made? One must also ask how low this given film dose can be made. It becomes obvious that there are two avenues toward dose reduction which we can broadly specify as (*A*) below the table and (*B*) above the table.

(*A*) *"Below the Table" Factors:* The primary factor here is the dose necessary to produce a desirable optical density on the film. For a given film-screen combination, this dose is essentially independent of tube kilovoltage over a wide range. Dramatic lowering of the dose is achievable, however, by the use of faster films and/or faster screens. Ardran (31, 32) has demonstrated this effectively over the conventional film-screen range. Table IX

TABLE IX: COMPARISON OF EXPOSURES WITH VARIOUS FILM-SCREEN COMBINATIONS

Film	Screen	Relative Skin Dose	mas
		r	
Standard	High definition	10.5	800
Standard	Par speed	4.2	320
Standard	High voltage	3.15	240
Ilford Red Seal	High voltage	1.57	120
Ilford Red Seal	Zinc sulfide	1.31	100

Lateral lumbar spine: 85 kv; 3 mm. Al added filtration; focal film distance 36-inch; P-B grid (Based on Ardran 31, 32).

is based largely on his data for lateral lumbar spine exposures and shows that by moving from a standard film-detail screen combination to a fast film-fast screen combination, patient exposure can be reduced by a factor of 8. His comparison, in American terms, is between Kodak Blue-Brand film plus Patterson detail screens and Royal Blue film plus Hi-Speed screens. Reference to Morgan (33) shows that the speed change would be from 200 to approximately 2,000, a factor of 10.

Very recently even greater speed gains have become possible. Very high-speed panchromatic emulsions which are sensitive in the yellow-green light range, *e.g.*, Royal-X Pan, have been developed. Such a film exhibits little speed gain if exposed with conventional blue-emitting calcium tungstate screens; but, if it is combined with a zinc sulfide screen, a further speed gain by a factor of 10 becomes possible. Gensini (34) has shown admirably, in a relatively crude first attempt, that 14 × 17-inch chest films are possible with fifteen times less dose than with a Blue-Brand/Par Speed combination. To illustrate the probable gain in the use of such a combination for abdominal films, Table X has been prepared, based on skin-dose measurements of Web-

TABLE X: PROBABLE REDUCTIONS IN PATIENT EXPOSURE DUE TO FAST SCREEN-FILM COMBINATIONS

Film	Screen	mas	Skin Dose	Ovary Dose
			r	mr
Blue-Brand	Par speed	60	0.6	125
Royal Blue	Par speed	30	0.3	62
Royal Blue	Hi-Speed	20	0.2	42
Royal-X Pan	CB2	4	0.04	8

Abdomen, Anteroposterior: 72 kv; 36 inches focal film distance.

ster and Merrill (20) and the relative speed measurements of Gensini (34). As the latter points out, a further speed gain is possible by double-coating the Royal-X Pan film.

"Cost" of Higher-Speed Film-Screen Combinations: The reduction of dose to the recording device inherently carries with it a reduction in the amount of information made available by the x-ray beam. The penalty paid for dose reduction at the recording device in radiography is similar to that paid in fluoroscopy. The latter has been elegantly analyzed by Sturm and Morgan (35) in a classical paper discussing the limits of screen intensification. Basically the limit lies in the fact that contrast perception depends not only on the difference in illumination level between adjacent areas, but also on the statistical variation in the illumination levels as more or less quanta arrive at the areas in question. For high illumination levels we may assume that the eye will perceive a difference between two illumination levels only if the difference between the mean illumination levels is greater than five times the standard deviation of those levels (36).

Let us apply this theory to detail perception in radiography. Sturm and Morgan have shown experimentally that the minimum object diameter perceptible at 10 per cent contrast on a radiograph with Blue Brand film and Par-speed screens is about 0.3 mm. The employment of a faster screen-film combination necessarily means that fewer x-ray photons are absorbed in it to produce unit photographic density. When the number of absorbed photons is reduced at the above 0.3-mm. diameter area, the statistical fluctuations become relatively larger. At 10 per cent contrast it will then only be possible to resolve a somewhat larger area receiving the same total number of photons as the smaller area previously. Hence, with the 16-fold speed increase discussed earlier, there will be an inherent reduction of area resolution by this factor; in other words, the minimum perceptible diameter at 10 per cent contrast is increased to 1.2 mm. This suggests that the line resolution may fall by a factor of 4, all other factors being constant.

The important sequel to this is that, in order to use really high-speed technics, the radiologist inevitably has to accept poorer detail resolution corresponding roughly to the square root of the speed gain. He therefore has to decide upon the examinations for which he is prepared to sacrifice the observed detail.

(B) "Above the Table" Factors: Confining ourselves here to radiography, the variables which control the skin/film dose ratio are the following: focal-skin distance, added filtration, and tube kilovoltage. Field size is also a variable but, assuming an efficient grid (an under-the-table variable) which removes most of the scatter, we can ignore it. It is here proposed to review the advantages to be expected from variation of these variables.

(a) Focal Skin Distance: Clearly the operation of the inverse-square law will reduce the ratio of skin to film dose as the tube focus is moved to a greater distance. This is exactly the same concept as treating patients at greater target-skin distances so as to improve depth dose. Unhappily the gains to be expected are quite small: *viz.*, moving the tube from 36-inch to 60-inch focal-film distance reduces skin dose by 25 per cent, and to 72 inches (impossible on present tables) by only 30 per cent. Dose reductions at the ovaries when these are in the useful beam will be even less (15 and 18 per cent, respectively). For lateral exposures, however, the advantages are greater: *viz.*, at 60 inches the skin dose reduction is

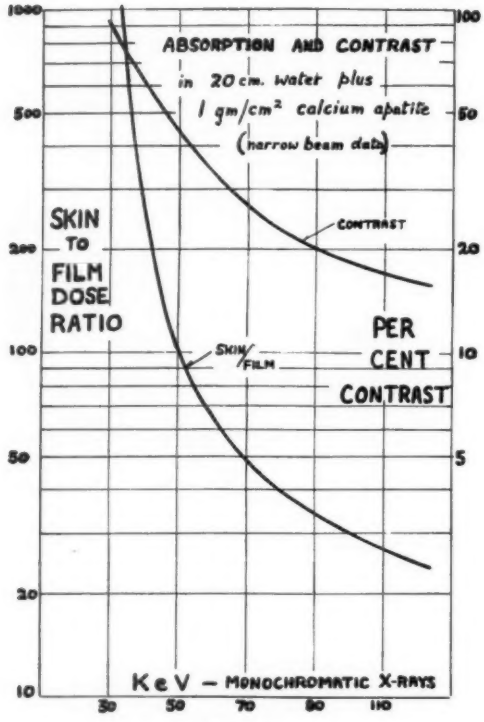

Figure 1.

42 per cent and at 72 inches 50 per cent, assuming a 14-inch lateral (hip) dimension. The ovary dose reduction will be about 25 per cent.

(*b and c*) *Added Filtration and Increased Kilovoltage:* The advantages of increases in both these variables have been shown conclusively by many investigators (4). Perhaps most startling are the results of Trout, Kelley, and Cathey (37), who for example show that the skin dose for a pelvic film at 60 kv is five times less when a 3-mm. Al filter is added, and that the skin dose for a pelvic film is reduced about twenty times by changing from 60-kv with 0.5 mm. Al filter to 130-kv with 0.25 mm. Cu filter.

One is provoked to consider what further gain is possible if primary radiation of even higher quality is used, *i.e.*, 200 kv with 1 mm. of copper added. That a further gain is possible is shown by Figure 1, which plots the ratio of skin dose (entrance) to film dose (exit) for a narrow monochromatic x-ray beam as the kilovoltage is increased. A body of water 20 cm. thick is assumed. Moving from 52 kev (h.v.l. 7 mm. Al) to 75 kev (h.v.l. 1 mm. Cu), a reduction of skin dose to one-half is possible. Confirmation of this for heterogeneous x-ray beams is found by comparing zero-field depth dose data for well filtered 130-kvp radiation with that for 200-kvp therapeutic radiation (50).

For this conclusion to be applicable to actual radiography with a screen-film combination and a Bucky grid, we must examine what happens to the film sensitivity at these higher qualities and determine whether the ratio of scatter to primary beam changes. The speed of a film-screen combination, or milliroentgens per unit photographic density, has been observed to remain essentially constant over the 60- to 130-kvp range (37, 39). The speed is primarily determined by the fractional energy absorption in the calcium tungstate screens, and this may be expected to continue its constancy almost up to 200 kvp. Mattsson (40), moreover, has shown that the proportion of scatter to primary radiation emerging from a thick phantom increases only about 15 per cent between 100 and 200 kvp. Hence, assuming a grid which maintains its opacity to scattered radiation up to 200 kvp, a progressive diminution in skin dose as kv is increased may be expected. Table XI summarizes these findings and includes the diminution of dose to be expected at the ovaries in obtaining an anteroposterior roentgenogram of an 18-cm. pelvis. This is calculated from wide-field depth dose data (37, 38). The table illustrates the rough expectancy that the reduction factor of dose to the ovaries is approximately the *square root* of the reduction factor to the skin.

Loss of Contrast at High Kilovoltage: It is a common observation that increase in the kilovoltage of an x-ray beam produces radiographs of lower contrast. This, of course, is unavoidable for bony and

TABLE XI: REDUCTION IN PATIENT EXPOSURE FROM HIGHER KILOVOLTAGE AND INCREASED FILTRATION

Kvp	60	60	85	130	200
Added filter (mm.)	0	3 Al	3 Al	0.25 Cu	0.5 Cu
Half-value layer (mm.)	0.8 Al	1.75 Al	2.5 Al	7 Al	1 Cu
Skin dose (mr)	2,700	600	400	140	70
Relative skin dose (%)	100	22	15	5	2.5
Ovary dose (mr)	210	133	118	64	42
Relative ovary dose (%)	100	63	56	30	20

18-cm. pelvis, anteroposterior study. Constant film density. 16:1 grid. (Based largely on Trout *et al.*, 37.)

other anatomic structures, since it is another manifestation of the lower absorption coefficients of tissue. This reduction is the price paid for a lower skin dose. The contrast produced by a given structure is proportional to the increased or reduced absorption of radiation in it compared with surrounding tissue. It is of interest to consider whether increased kilovoltage reduces contrast to the same extent that skin dose is reduced. For this purpose the relative absorption and hence the contrast offered by about 5-mm. thickness of bone has been calculated for monochromatic x-ray beams and plotted in Figure 1. The absorption was calculated for 1 gram sq. cm. of calcium apatite $Ca_{10}CO_3(PO_4)_6$. It will be noted that contrast falls off more slowly than does skin exposure, particularly over the low voltage range. In the voltage range above 50 kv (effective), however, the reduction of skin dose is almost parallel to the reduction of contrast. Since only a certain minimum contrast can be distinguished by the eye (approximately 2 per cent) this means that the lower contrast detail is progressively lost from view as the kilovoltage is raised. It is difficult to estimate the exact loss of contrast over a given range of heterogeneous radiation from this curve; assuming that it is the *exit* qualities of radiation which must be compared, it appears that contrast will fall in a 3:2 ratio as the kvp is increased from 130 to 200 kv. This should be compared with a 2:1 reduction in skin dose. It is assumed that the same proportion of scatter to primary reaches the film.

(*C*) *Other Factors in Dose Reduction:* The importance of shielding the male gonads has been discussed by numerous authors. If it should prove, as suggested by Carter (41) but disputed by Russell *et al.* (18), that the male is more mutable than the female, such shielding would represent a method of removing the major part of genetic risk from radiologic examinations. Simple shields which may reduce testicular exposure 100-fold have been described in the literature (42, 43).

The dose to the gonads will also be reduced on two counts by minimizing field sizes. If the field is centered near the gonads, a reduction in its size might remove the gonads from the useful beam. Alternatively, if the gonads are normally outside the useful beam, a reduction of scattered radiation will occur to an extent *greater* than the area reduction. Haybittle (39) and Webster and Merrill (20) have indicated how scatter dose falls off rapidly with distance from the edge of the geometric beam, a threefold reduction being achieved for a 2-inch increase in distance.

CONCLUSIONS

The hazards of diagnostic radiography to the patient, even by the most pessimistic standards, are small. They are low enough to be outweighed by the expectation of a small potential benefit. The somewhat larger genetic hazards of most examinations are surpassed by those accruing from wearing a radium-dial wrist watch and, apparently, from wearing trousers. In the case of mass chest surveys a comparison of benefit and damage is theoretically possible; a preliminary consideration indicates a large balance of benefit if well coned x-ray apparatus is used.

Large reductions of dose are technically possible through several approaches, no-

tably the use of increased kilovoltage and new faster film-screen combinations. By these means together, a factor of 100 reduction may be achieved compared with levels common today, although the full realization of this may depend on the development of green-emitting screens with high atomic number. The cost of such a reduction is a marked loss of detail and contrast. The radiologist must decide upon the circumstances and the examinations in which the quality of a roentgenogram may legitimately be sacrificed in the interest of minimum hazard.

APPENDIX

Possible Relation Between Cancer Incidence and Leukemia Incidence

In the cases of thymic enlargement treated by irradiation in infancy in which subsequent leukemia and other malignant diseases developed (7), the typical roentgen factors were: 120–130 kvp with 3 to 5 mm. of aluminum added filtration, a treatment distance of 30 to 40 cm., and a field size of 10 × 10 cm. essentially covering the whole chest in these infants, nearly all of whom were less than two months old. The midplane dose (5 cm. deep) is about 50 per cent of the skin dose. On the other hand, the mean bone-marrow dose is taken to be 25 per cent of the skin dose, on the assumption that the ribs, sternum, and dorsal spine contain about 40 per cent of the active marrow (4, page 64). Since the cases of leukemia and of other malignant disease are about equal in number, the cancer rate per rad of midplane dose is about half the leukemia rate per rad of mean bone-marrow dose.

One possible method for the extrapolation of this cancer rate to diagnostic radiography in adults depends on the following two pessimistic assumptions: (*a*) that the dose-effect relation is linear and (*b*) that the integral dose relative to the body weight is the important dose parameter; *i.e.*, the average whole-body dose.

The half-value layer for the radiation used in the infant treatment is about 6 mm. Al and the half-value thickness of tissue is about 4.8 cm. (50). Using Mayneord's formula, we derive an integral dose of about 1,000 gm.-rad per skin rad; or 2,000 gm.-rad per rad to the midplane. Assuming a mean weight of 10 lb. for these infants, the average whole-body dose was 0.44 rad per rad to the midplane.

A 14 × 17-inch diagnostic film of an adult 20 cm. thick at 36-inch focal-film distance exposes a skin area approximately 10 × 12 inches, or approximately 800 sq. cm. At 70 kvp with 2 mm. of aluminum added filter, the half-value thickness of tissue given by Trout *et al.* (37) is 4.3 cm. and the 10-cm. depth dose about 20 per cent. The integral dose per skin rad will be about 6,000 gm.-rad or 30,000 gm.-rad per rad to the midplane. Assuming a body weight of 70 kg., the average whole-body dose is 0.43 rad per rad to the midplane.

Because of the similarity of the average whole-body doses per midplane rad, the cancer rate relative to the leukemia rate derived for the infants, is applied to the case of large-field adult diagnostic radiography.

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(For Discussion of this paper, see page 528)

(Pro le summario in interlingua, vider le pagina 532)

The Elusiveness of Neoplasia Following Roentgen Therapy for Thymic Enlargement in Childhood[1]

LEONID S. SNEGIREFF, M.D.[2]

THE PRACTICE of irradiating enlarged thymus glands in infants and children began a little over a half century ago (1) and at the time was considered a great stride forward in the effort to reduce the hazard of status thymicolymphaticus. Prior to this, surgery was the principal method of treatment, offering the alternatives of exopexy or the excision of the enlarged thymus gland. One can still remember vividly the dilemma which confronted those who treated children before antibiotics became a part of our therapeutic armamentarium; the sudden death of an infant from suffocation was witnessed all too often. According to Marine (2), who gives an excellent review of the whole subject of status thymicolymphaticus and *mors thymica*, the priority for having described this entity goes to Felix Plater. Plater in 1614 reported the sudden death of a boy of five months, with thymic enlargement found at necropsy, and referred to 2 other boys in the same family dying suddenly with the same symptoms. For over three hundred and twenty-five years, unwarranted publicity was given the assumption that thymic enlargement accounts for much mortality in infancy and childhood. The whole controversial subject of status thymicolymphaticus was debated for years with much heat and little light, by protagonists like Symmers (3) and antagonists like Greenwood and Woods (4) and Young and Turnbull (5), who collected and analyzed many different data.

It was particularly difficult to refute certain generalizations which were supported by evidence based on careful observations of outstanding clinical teachers. Chevalier Jackson, for example, in 1907 demonstrated an enlarged thymus roentgenographically, which on bronchoscopic visualization was shown to produce a scabbard deformity in the trachea (6).

The use of ionizing radiation as a prophylactic measure against status thymicolymphaticus in infancy and childhood gained in popularity in many areas during the succeeding years. It should be emphasized, however, that there always existed nuclei of opposition to this practice. Kennedy and New (7) pointed out that chronic stridor in childhood need not be attributed to thymic enlargement and discouraged the use of irradiation. Eventually, the pendulum did swing away from roentgen therapy, particularly after abandonment, on scientific grounds, of the belief in sudden death from status thymicolymphaticus as a commonplace occurrence. Additional evidence came to light with autopsy demonstration of extensive microbial infections of the respiratory tract associated with episodes of sudden death (8).

Over the years suspicion mounted that some latent untoward effects were associated with previous exposure to ionizing radiation; this, in turn, led to a number of studies on patients who developed such diverse sequelae as aplastic anemia (9), carcinoma of the thyroid (10), acute leukemia, and other forms of neoplasia (11, 12).

I became interested in this problem and checked available data in several teaching hospitals in the geographic area of Boston for suitable groups of patients to study.

[1] Presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Nov. 16–21, 1958.

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This study was made possible by Project #CS-9430, National Cancer Institute, Department of Health, Education, and Welfare, Public Health Service.

A single institution was selected for the primary study because it had the following characteristics: a large out-patient department service; a uniform practice, dating back to 1932, of roentgenologic evaluation for thymic enlargement prior to the acceptance of children for tonsillectomy; a uniform method of roentgen treatment of enlarged thymus glands since 1926, continued for over two decades under the supervision of the same radiologist; adequate comparison groups of patients with similar environmental background and, except for the enlarged thymus gland, patterns of illness and of relative tonsillar hypertrophy resembling those found in the group of patients treated by roentgen rays.

After a preliminary study of the raw data in the daily log of patients admitted for a roentgenographic appraisal of the thymus, all available information was typed on 5 × 8-inch cards. The medical record of each patient was studied; the major findings including therapy and dates of visits were recorded.

Intensive follow-up was instituted to locate the patient or his immediate family. This included a check, carried out by the same staff in our department, of telephone and city directories and police listings and visits to former neighbors at the last known address of the patient. In addition to the above normal channels for tracing patients, the Massachusetts Public Health Department Cancer Clinic files and the State Death Registry were checked against the list of patients.

Two principal groups of patients are considered in this study: the thymus-irradiated group and the comparison, non-irradiated control group. Both groups came, without preselection other than availability, from the total list of patients entering the out-patient department service of the institution because of enlarged tonsils and repeated eye, ear, nose, and throat infections during the years 1923 to 1947. The physical appraisal included a roentgenogram of the thymus gland. There was automatic referral of thymus positives for radiation therapy, *i.e.*, patients found to have an enlarged thymus gland were referred to the roentgenologist for a course of treatment prior to their acceptance for tonsillectomy or other definitive surgical treatment.

In addition to the principal group of irradiated patients with enlarged thymus, there is a small subgroup whose roentgenograms showed an enlarged gland or a suspicious borderline enlargement who refused or were not given roentgen therapy. The groups and the subgroup matched very closely in respect to age at the time of the first roentgenogram.

This preliminary report is based on findings extracted from medical histories and through follow-up of the first 148 patients of a possible total of 1,131 who had ever received roentgen therapy for thymic enlargement; 23 of the possible total of 269 nontreated patients with enlarged thymus gland; 162 of the nontreated patients who showed no enlargement of the thymus roentgenographically prior to tonsillectomy in childhood. The latter group of 162 patients is a part of a possible total of 7,000 persons ever admitted for tonsillectomy. Simultaneous follow-up was instituted in both the thymus-irradiated patients and the controls.

Method of contact was by personal visit of a trained follow-up worker to all patients residing in Greater Boston and nearby communities, wherever this was possible. Those who lived at a greater distance were interviewed by letter and by telephone.

In all correspondence, the letterhead of the Gerontology Unit at the Harvard School of Public Health was used; the initial letter read as follows:

Dear_____:

We are asking your help in the search for answers to better health for the children of Massachusetts. As parents of a child who has attended a hospital out-patient clinic some years ago, it is possible that you may have information which will help us to understand more fully the long range effects of eye, ear, nose, and throat treatment of children. Scientists in different hospitals are comparing the results of treatment of children by different methods. With

your help we, too, will be able to contribute to this growing knowledge.

A little of your time in completing the enclosed questionnaire makes the difference between knowledge and ignorance in this case. We are enclosing a self-addressed envelope for your convenience in returning the completed questionnaire to us.

We earnestly ask for your assistance in this study. The facts which you give us will, of course, be held confidential; we hope that this information may lead to a better understanding of the treatments which make for a healthier person.

Sincerely yours,
L. S. SNEGIREFF, M.D.
Associate Professor

Your child was treated at_____Hospital on_____.

HEALTH QUESTIONNAIRE

Information about_____
What is your daughter's present address?_____
Please check if your daughter developed any other serious illness and, if so, can you give the approximate dates or age of your daughter when diagnosed:_____
Did any other children in the family develop similar illnesses? If yes, who and, at what age?_____

Did your daughter have any of the following diseases:

Allergy: hay fever, food or cosmetic allergies ☐
Pneumonia: ☐
Heart Disease: ☐
Diabetes: ☐
Tuberculosis: ☐
Other Chronic Diseases: ☐
Polio: ☐
Any special treatments such as: Surgical ☐ X-Ray ☐ Penicillin ☐

If your daughter was ever anemic, did she have blood tests done?
Were blood tests done in a hospital?
What did they show?
Where were they done?
Was there ever a biopsy done?
Any diagnosis of leukemia or tumors of any kind?
How many colds does your daughter have in a year?

What is your daughter's doctor's name?_____
Street City State
Do you know when your daughter last saw her doctor?
Was your daughter in military service?
Did your daughter have any illnesses in military service? If any, please state which, when, and where

Please mention if your other children have any particulars of medical interest?_____

Is your daughter married? If so, what is her married name?_____
Did or does your daughter have difficulty with her monthly (menstruation) periods?_____

Has your daughter had any children?_____
Any miscarriages?_____
If so, please give details concerning pregnancy (date when delivered each time, condition of child, etc.) (If necessary, please use reverse side.)
Information about_____
What is your son's present address?_____
Please check if your son developed any serious illness and, if so, can you give the approximate dates or age of your son when diagnosed:_____
Did any other children in the family develop similar illnesses? If yes, who and at what age?_____

Did your son have any of the following diseases:

Allergy: hay fever, food or cosmetic allergies ☐
Pneumonia: ☐
Heart Disease: ☐
Diabetes: ☐
Tuberculosis: ☐
Other Chronic Diseases: ☐
Polio: ☐
Any special treatments such as: Surgical ☐ X-Ray ☐ Penicillin ☐

If your son was ever anemic, did he have blood tests done?
Were blood tests done in a hospital?
What did they show?
Where were they done?
Was there ever a biopsy done?
Any diagnosis of leukemia or tumors of any kind?
How many colds does your son have a year?
What is your son's doctor's name?_____

_____
Street City State

Do you know when your son last saw his doctor?
Was your son in military service?
Did your son have any illnesses in military service? If any, please state which, when, and where _____

Please mention if your other children have any particulars of medical interest? _____

The treatment of patients found to have enlarged thymus glands was individualized after appraisal by the roentgenologist of the general physical condition, in the light of the roentgen findings, with due consideration of the size of the thymus in relation to the total-body size.

The estimated dosages for treatment of patients in the study group were given in accordance with the following schedule: 100 r per single treatment, 200 r for two treatments, and a total of 350 r in three treatments, while those who did not show the expected response were given a double course of therapy which averaged 600 r. The interval between treatments was ten days.

The anteroposterior portal was measured and a suitably sized cone selected to meet the individual requirements of each infant or child. The largest portal used measured 12.7 cm. in diameter. Erythema was never observed in any of the infants and children following the above mentioned courses of therapy.

From 1924 to 1935, a Wappler unit of 100 kv capacity was used, while from 1935 to 1946 a Westinghouse unit of 100 kv capacity was in operation. In 1946, treatment for enlarged thymus gland was discontinued following a change in institutional policy.

In this study, we found that 87.83 per cent of the thymus-irradiated group received a total of 400 r in four separate exposures of 100 r at ten-day intervals; 7.42 per cent received 1,200 r; 1.35 per cent received a single treatment of 100 r, while the remaining 3.39 per cent received multiple doses varying from 350 to 1,800 r total. It will be noted that only 6.76 per cent of patients in the thymus-irradiated group were under one year of age, while 74.32 per cent were three years of age and older at the time of treatment.

The nonirradiated comparison group with normal sized thymus glands shows similarity in age and sex. The subgroup of non-irradiated children with enlarged thymus glands shows an age distribution of 13.04 per cent under one year, while 65.22 per cent were three years of age and older.

The population sample in this study

consists of 344: 333 are alive and well, as far as can be determined, 2 are alive and not well, 9 are dead. Of the 333 who are alive and well, 180 are males and 153 are females.

To date, our findings are essentially negative with regard to malignant neoplasia in all patients interviewed. However, we did find 2 patients with disease that may be connected with previous roentgen irradiation; 1 with thyroid adenoma and 1 with "cystic thyroid"; both are being studied.

Complementary to our findings are those in a recent and as yet unpublished survey of another hospital population group in the Boston area studied by William Moloney (13). In a group of 99 patients with adequate follow-up, from a total of 700 patients who originally received x-irradiation for thymic enlargement in infancy and childhood, 92 are living. Of these, 69 are well; in 16 some illness believed unconnected with x-radiation has developed, while 7 have disease probably connected with roentgen therapy. Of the 7 dead, only 2 had neoplasia possibly attributable to radiation exposures. Moloney found that about one-third of the group exposed to radiation were under one year of age; 66.6 per cent of these received 150 r, 6.7 per cent received 50 r, and 26.6 per cent received over 150 r. Over 68 per cent of the total group (99 cases) were given a total of about 150 r. With reference to the latency period for thyroid carcinoma, in a recent study Wilson *et al.* (14) found that, following x-irradiation in the first year of life, signs failed to appear before ten to eighteen years. This paralleled the experience of patients receiving x-radiation in adolescence, in whom the latency period varied from eight to seventeen years.

TABLE I: DR. MOLONEY'S SERIES: 99 CASES OF THYMUS IRRADIATION IN CHILDREN

Age	Living: 92 Patients (92.92%)		Dead: 7 Patients (7.07%)		Total Number
	Possible Cancer-Connected Illness	Well or Unconnected Illness	Cancer-Connected Deaths	Unconnected Deaths	
Under 1 year	2 (2.02%)	24 (24.24%)	1 (1.01%)	3 (3.03%)	30 (30.3%)
Over 1 year	5 (5.05%)	61 (61.61%)	1 (1.01%)	2 (2.02%)	69 (69.69%)

The careful study of these data is indeed revealing, bringing into focus the several variable factors such as age, dose, and latency period within the particular groups of children studied. In addition, one must learn from the observations which are already available on large population groups in given geographic areas. For example, the age-adjusted morbidity rates for primary cancer of the thyroid are inconstant—2.1 for the northern states, in contrast to 4.1 for the western states and 1.6 for the southern (15). The expected incidence of thyroid cancer in the western states is almost twice that in the northern states. Such observations do not detract from the importance of special studies of small groups of patients, like that reported here. Limited hospital samples offer an opportunity for the intensive analysis of the variable factors mentioned above, including age, roentgen dose, and technical problems connected with treatment and follow-up. But it is important to avoid indiscriminate pooling of small samples drawn from hospital experience in widely separated parts of the country unless the specific risk of development of primary cancer in a given area is taken into account and is given proper statistical weight. The selection of comparison or control groups from the same population sample as the original study group is axiomatic.

To shed further light on the frequency with which malignant neoplastic processes, such as acute leukemia in children, may be associated with exposure to ionizing radiation in the total perspective of all factors with possible etiologic significance

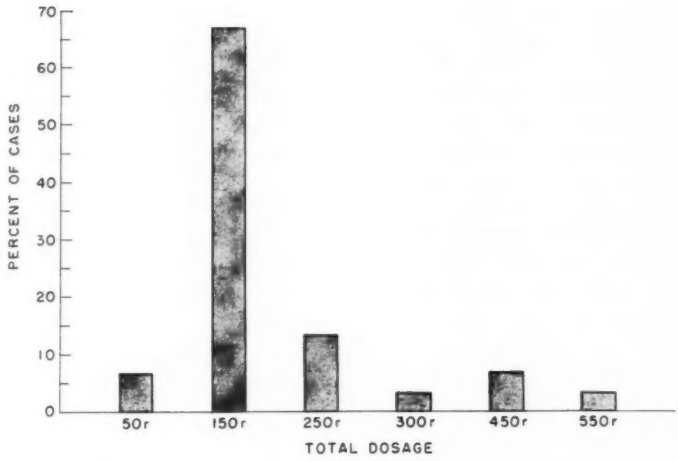

Fig. 1. Dr. Moloney's series. Thymus-irradiated group under one year of age: 30 cases. Percentage distribution by amount of radiation: 50 r, 6.7 per cent; 150 r, 66.6 per cent; 250 r, 13.3 per cent; 300 r, 3.3 per cent; 450 r, 6.7 per cent; 550 r, 3.3 per cent.

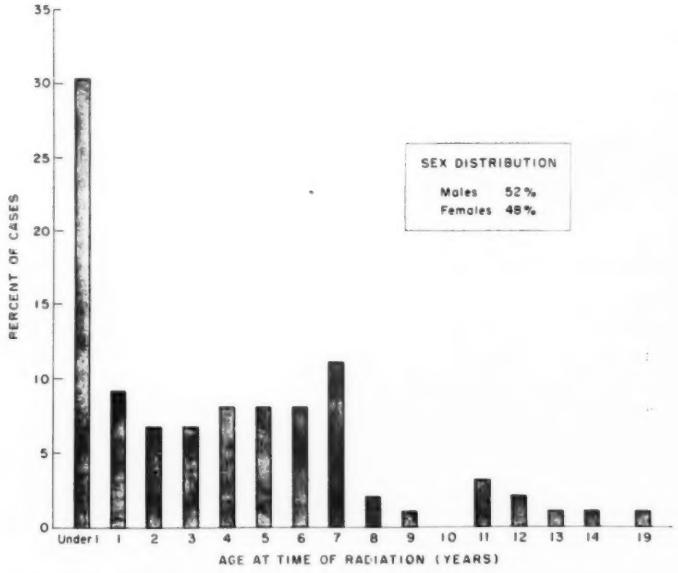

Fig. 2. Dr. Moloney's series. Thymus irradiation in children: 99 cases. Age and sex distribution. Under one year of age, 30.3 per cent; one to two years, 9.09 per cent; two to three years, 7.07 per cent; three to four years, 7.07 per cent; four to five years, 8.08 per cent; five to six years, 8.08 per cent; six to seven years, 8.08 per cent; seven to eight years, 11.11 per cent; eight to nine years, 2.02 per cent; nine to ten years, 1.01 per cent; ten to eleven years, 0 per cent; eleven to twelve years, 3.03 per cent; twelve to thirteen years, 2.02 per cent; thirteen to fourteen years, 1.01 per cent; fourteen to fifteen years, 1.01 per cent; nineteen years, 1.01 per cent.

we turned to the records of the Tumor Clinic at the Children's Cancer Research Foundation in Boston (16) where, between Jan. 1, 1947, and Nov. 1, 1958, 856 cases of acute leukemia were diagnosed and followed. Eleven patients from this group are known to have had roentgen therapy in infancy for nonmalignant disease. Of the 11, 5 were treated for enlarged thymus gland. Their age at the time of roentgen therapy ranged from one week to five months, while the age at the time of diagnosis of leukemia was between two and one-half years and eight years. Only 1 of the 5 was a female (17).

Even if we assume that the memory of some of the respondents is not completely accurate and that with others the reference may have been accidentally omitted, there is still a vast numerical difference between the principal factors precipitating leukemia: in the 11 patients it was the ionizing radiation in infancy; in the remaining 845 patients, the precipitating factor is unknown. On the other hand, if this is a representative sample, which I believe it is, then the risk of leukemia developing in children as a result of clinical irradiation of the thymus gland, in contrast to other precipitating factors, is relatively small: 5 in 856, or a rate of 0.0058.

This makes one ask whether in the past, through lack of simultaneous follow-up of identical populations of roentgen-ray-treated and properly chosen control groups, the problem of the impact of thymic radiation may have been exaggerated beyond reasonable perspective. Few will disagree, however, that exposure of infants to therapeutic doses of ionizing radiation in nonmalignant disease, unless for sound clinical reasons, is to be discouraged, for it must of necessity carry a certain calculated risk and danger of development of malignant neoplasia.

At present we have evidence that the danger of development of primary thyroid cancer varies appreciably in different sections of the United States, being almost twice as great in the western as in the northern states. In assessing the risk of development of malignant change in the thyroid following exposure to roentgen therapy in childhood, due weight must be given to the prevailing general risk of thyroid cancer which exists in the geographic area whence the hospital sample is drawn. The same holds true for acute leukemia, where accurate base-line figures

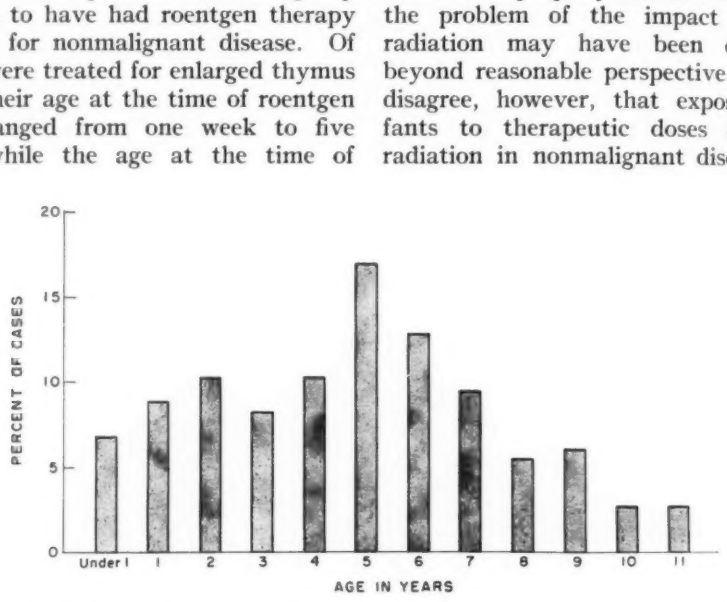

Fig. 3. Author's thymus-irradiated group: 148 cases. Percentage age distribution at time of roentgenogram: under one year of age, 6.76 per cent; one year, 8.78 per cent; two years, 10.14 per cent; three years, 8.11 per cent; four years, 10.14 per cent; five years, 16.89 per cent; six years, 12.84 per cent; seven years, 9.46 per cent; eight years, 5.41 per cent; nine years, 6.08 per cent; ten years, 2.70 per cent; eleven years, 2.70 per cent.

await collation of currently assembled data by the Public Health Service, Department of Health, Education, and Welfare.

Until new data are made available by the systematic pooling of large cross sections of experience, with adequate follow-up, in each part of the country, there will continue to exist considerable differences in the individual reports; these differences depend on the particular sample and the clustering of several variables previously discussed.

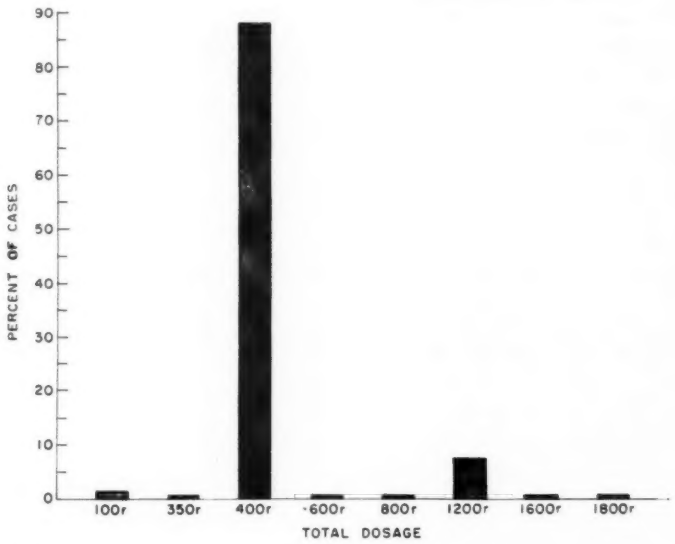

Fig. 4. Author's thymus-irradiated group: 148 cases. Percentage distribution by amount of radiation (total dosage). One treatment, 1.35 per cent; 3 treatments, 0.68 per cent; 4 treatments, 87.83 per cent; 6 treatments, 0.68 per cent; 8 treatments, 0.68 per cent; 2 treatments (double), 7.42 per cent; 2 treatments (double) and 4 treatments (single), 0.68 per cent; 3 treatments (double), 0.68 per cent.

The studies reported here point to a definite need for registries of persons exposed to clinical x-radiation in different parts of the United States; hospital registers can facilitate follow-up of patients and contribute to more accurate knowledge of the associated morbidity and the eventual outcome. At present, the full significance of the impact of clinical radiation is difficult to quantitate because of a number of variables which exist in each of the samples reported in the literature.

You are well aware that some of the factors which recur in the association of roentgen therapy of enlarged thymus gland in infants and children with subsequent development of malignant neoplasia are:

(*a*) Age of infant or child at the time of exposure

(*b*) Total radiation dose delivered; the specific length of intervals between the several doses given in the course of therapy

(*c*) Expertness in protecting large parts of the body of the infant or child against unintended exposure

(*d*) Additional factors which require more subtle methods of appraisal through prospective, rather than retrospective epidemiological studies, as the state of endocrine development, as well as possible pathological processes such as virus infections, which may be under way during roentgen therapy. Special effort must be made to track down all exposures to ionizing radiation: clinical, industrial, and avocational, for, not infrequently, some exposures go unrecorded as, for example, the use of fluoroscopy in shoe-fitting.

Where possible, data on occupational and personal habits must be included, especially since sooner or later lung cancer may develop in a number of these patients and we will be faced with the problem of determining the principal precipitating factor in a complicated picture of causal associations.

It is obvious that our data do not bear out the high incidence of cancer following x-irradiation for enlarged thymus gland in infancy and childhood, previously documented in medical literature (11, 12). Comparison with another recent, heretofore unpublished hospital survey in our geographic location (13) indicates a closer approximation of experience in these more uniform though small samples of hospital population. In contrast, one can appreciate how easy it is to reverse the experience; were one to add a sample of 5 patients seen in a tumor clinic of a third hospital in the same geographic area, where children had received x-radiation outside but had come to the clinic for other treatment, there would be an obvious bias introduced, with resultant change in observed cancer incidence. This type of stacking of regional experience is obviously unacceptable, but it points to the fact that it is possible for other bias to creep in through regional geographic differences in respect to the risk of development of primary cancer of the thyroid.

The observation of 2 patients with benign thyroid disease is an indication of the necessity to continue follow-up of both the treated and the control groups, for it is possible that our experience with the sample under study may change in the future. It is important to realize that statistical bias may result from introduction into a hospital study of added samples of referred patients from private pediatric or roentgenologic practices with different economic variables or from the tumor clinics in the same or in different geographic areas, or through failure to elicit history of nonclinical exposure to ionizing radiation.

Only a relatively complete pooled sample of total clinical experience in a given geographic area, compared with a study of the total demographic experience in the area for given periods of time, can give an accurate picture of the role played by ionizing radiation in the total picture of cancer in each primary site.

SUMMARY AND CONCLUSIONS

A preliminary report has been made of a study of 148 persons who received roentgen irradiation in childhood and infancy because of an enlarged thymus gland, a group of 23 untreated patients with thymic enlargement, and a comparison group of 162 patients without detectable enlargement of the thymus. All were examined and followed in the same medical institution. To date, no malignant neoplasms have been found, although 75 of the 148 patients treated for an enlarged thymus have been followed for over twenty years. In 2 patients benign thyroid conditions have developed: adenoma and cystic disease, 1 each. Three have died of nonmalignant disease. A control group of 162 patients likewise showed no cancer; there were 6 deaths, all from nonmalignant disease. Our observations are supplemented in essence by other data from our geographic area, as yet unpublished.

The previously reported high incidence of primary cancer of the thyroid and of leukemia following irradiation for thymic enlargement is not borne out in our sample. Some of the contributing factors to observed differences include such variables as age at the time of roentgen therapy, total roentgen dose, interval between multiple doses, duration and completeness of observations, sex of patient, the total time of follow-up, selection of comparison or control groups from particular geographic areas, general liability to risk of cancer in a particular primary site, possible differences in economic variables.

There is need for systematic registration and complete follow-up of all patients exposed to therapeutic doses of ionizing radiation for conditions other than malignant disease. The follow-up ideally should

be continued for the lifetime of the patient; hence, there should be regional registries in representative areas of the nation.

Much of the elusiveness in the study of neoplasia following roentgen therapy for thymic enlargement in childhood is traceable to the variables which occur in the selection of patients, the composition of groups, the age at time of treatment, and the dose given in different studies.

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(*For Discussion of this paper, see page 528*)

(*Pro le summario in interlingua, vider le pagina 533*)

Genetic Effects in Children and Grandchildren, of Women Treated for Infertility and Sterility by Roentgen Therapy

Report of a Study of Thirty-Three Years[1]

IRA I. KAPLAN, M.D., F.A.C.R.

THE DEDUCTIONS of the experimental geneticists are questioned by many because of the almost total absence of valid data concerning radiation-induced genetic damage to human offspring. In the present paper an analysis is made of the genetic changes observed in two successive generations of the offspring of 644 women who had received roentgen therapy for a tissue dose of approximately 65 r to the ovaries and 90 r to the pituitary, with a follow-up in over 50 per cent of the cases of five to thirty-two years.

MATERIAL

During the past thirty-three years there have been referred to the author 825 women for roentgen therapy for sterility; 800 have been treated. The statistical data are as follows:

Number of married women referred for treatment	825
Number not accepted for irradiation	25
Number of women irradiated	800
Number treated and not traced	156
Number of patients treated and followed	644
Number of these women who conceived	351
Number of conceptions	688
Number of children born alive and normal	543
Number of children born dead or died some time after birth	20
Number of children born alive with abnormalities	3
Number of children died by accident	2
Number of married children producing grandchildren	35
Number of grandchildren born	45

All of these women were referred by gynecologists, only after all other methods for the relief of sterility had been tried and had failed. The diagnosis of sterility was made by the referring physician, after performance of the usual diagnostic tests for sterility. In most instances the husbands had also been tested.

The age of the women treated ranged from eighteen to forty-two years. In 277 of the series irregular menstruation was associated with sterility. In 64 patients menstruation was regular.

The period of sterility prior to treatment ranged from one to nineteen years. Fifty-seven per cent of the patients were sterile from four to ten years and 43 per cent from eleven to nineteen years. In 5 patients there was a second marriage before irradiation treatments were instituted. In 60 cases the patient had previously conceived; 21 of this number had borne a child and 39 had miscarried and failed to conceive again until after irradiation. (The 21 children previously born to these women are not included in any statistical data of this presentation.)

METHODS

High-voltage irradiation has been employed consistently over the past thirty-three years, with the following factors: 200 kv, 1 mm. Cu h.v.l., 50 cm. distance, 8 × 10-cm. portals for the pelvis and a round portal 5 cm. in diameter for the pituitary area. Treatments are given in three sessions at seven-day intervals with an overall time of fourteen days. At the first session, 50 r, measured in air, is administered to the right and left anterior pelvic areas, and 75 r, measured in air, to the central forehead, with the rays directed to the pituitary. Seven days later, 75 r, measured in air, is given to the right and

[1] Presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16-21, 1958.

Reference to the work of others in the field has been purposely avoided; this paper is concerned solely with the results of the author's own studies.

left posterior pelvic areas, and 75 r, measured in air, to the central forehead. At the final session treatment similar to that of the first day is administered to the anterior pelvic areas and the forehead.

With this procedure, the mean total tissue dose to each ovary is approximately 65 r, measured with back-scatter, in fourteen days. Because of the variation in the dimensions of the pelvis, the range was approximately 50 to 90 r. The mean total dose to the pituitary was about 90 r in the fourteen days. This procedure was fairly constant for most patients.

During the past two years an intensive study of these patients was carried out and 644 of the 800 women treated were traced. Contacts were made directly with the patients by mail, telephone, through the referring physician, bureaus of vital statistics, obstetricians and obstetrical clinics, etc. Approximately 95 per cent of the successfully irradiated women supplied photographs of their children and grandchildren. Inquiry was made on the scholastic ability of about 90 per cent of the children; in only 1 child was retardation noted.

OBSERVATIONS AND RESULTS

Observations are based on 644 irradiated women who were followed for periods ranging from one to thirty-three years. Three hundred and fifty-one of these women had 688 pregnancies, and 293 failed to conceive following irradiation.

Of the 351 irradiated women who conceived, 318 bore 566 children, 282 males and 284 females. One hundred and thirty-seven bore 1 child, 125 bore 2 children, 45 bore 3 children, and 11 bore 4 children.

There are 543 *normal healthy living children* of the 566 born to the 351 women who conceived: 260 boys and 283 girls, including 5 sets of twins. Twenty children died at or after birth and 3 children are alive with abnormalities.

Children born dead at term are considered *stillbirths*. They constituted 1.4 per cent of all births: 4 were due to strangulation from cord entanglement and 4 to other causes.

Stillbirths due to cord strangulation	4
Stillbirths due to hydrocephalus	3
Stillbirths due to maldevelopment (result of large uterine fibroid)	1

There were 12 *deaths* of living children: 3 following premature birth; 2 from congenital abnormality; 2 after an automobile accident; 1 from surgery for Hirschsprung's disease; 1 from pneumonia four days after birth; 1 from Tay-Sachs disease (with a familial history in both parents); 1 from tetanus infection at six years of age; 1 from drowning at two years of age.

The October 1958 report of the National Office of Vital Statistics shows a fetal death rate of 16.6 per cent. In this series the rate is 20.6 per cent; it should not be overlooked, however, that these women were not deemed normal before therapy.

It is known that women referred for irradiation for sterility have some ovarian dysfunction and undeveloped uteri and are prone to miscarriage. In the present series 91 women *miscarried*, some more than once, but 68 of these again normally conceived and bore children Seven women conceived but the pregnancy was ectopic and had to be terminated. One of these women has subsequently borne 2 normal children.

The figures for deaths and miscarriages are as follows:

Total conceptions	688	
Deaths	143	(20.6%)
Stillbirths and deaths of living children	20	
Miscarriages	123	(17.7%)
No. of women who miscarried	91	(14.1%)
No. who again safely conceived	68	
No. who failed to conceive again	23	

Abnormalities occurred in but 3 living children born following irradiation of the mothers. These instances may perhaps suggest evidence of some genetic influence. The details of these cases are as follows:

Mrs. G. C., irradiated Feb. 26, 1952, bore a normal baby on June 30, 1953, and then on Nov. 17, 1955, bore a child with but one finger on one hand and one toe on one foot.

Mrs. E. K., irradiated Sept. 1, 1950, bore a normal baby boy March 18, 1952, and on Aug. 21, 1954, gave birth to a second son who has slight mental

TABLE I: SUMMARY OUTLINE OF THE FOLLOW-UP OF 644 IRRADIATED WOMEN

A. 644 women irradiated and followed, 1925–1958
   1. Became pregnant ..... 351 — Number failed to conceive 293
   2. Number of pregnancies 688
   3. Number who bore children 318
   4. Number of children born 566
B. Women who became pregnant but failed to deliver normal children
   1. Number who miscarried and failed to bear children 23
   2. Number with ectopic pregnancy 7
   3. Number who bore dead children 8
      (*a*) From strangulated cords 4
      (*b*) From hydrocephalus 3
      (*c*) From maldevelopment due to large uterine fibroid 1
C. Report of 566 children born
   1. Number living: 545 (including 5 sets of twins)
   2. Number died: 20
      (*a*) Stillbirths (group B) 8
      (*b*) Other causes 9
      (*c*) By accident 2
         By drowning at two years of age
         By tetanus at six years of age
      (*d*) Tay-Sachs disease 1
D. Abnormalities of first-generation children: 3 (all living)
   Living with genetic abnormalities
      (*a*) Boy with one finger on one hand and one toe on one foot
      (*b*) Girl with extra thumb on one hand
      (*c*) Boy with premature closing of fontanelles
E. Married children and grandchildren of irradiated mothers
   1. Number of children married 35
      Girls, 21
      Boys, 14
   2. Number of grandchildren born: 45
      Boys, 23
      Girls, 22
      (one set of twins—boy and girl)
   3. Number of grandchildren living 44
      Number of grandchildren dead .... 1 (from maternal eclamptic toxemia)

TABLE II: STATISTICAL SUMMARY

	Normal %	This Series %
Sex ratio	50–50	50.2–49.8
Miscarriage rate	10+	17.7
Fetal death ratio	16.6	20.6
Stillbirths	4	1.4
Known abnormalities	4.2–7	1

retardation due to premature closure of the fontanelles.

Mrs. E. B., irradiated Sept. 14, 1951, bore a baby girl on May 6, 1957, having six fingers (an extra thumb) on one hand.

Grandchildren of the Women Irradiated for Sterility: It has been said that irradiation of females tends to create a condition of sterility in their progeny. To date this has not been evident in the author's series. At present 35 children (14 men and 21 women) of these irradiated women are married and 31 of these already have had a total of 46 normal children, that is, grandchildren of the originally irradiated women. Forty-five of these (25 boys, 20 girls) are alive; 1 died shortly after birth as a result of maternal eclamptic toxemia.[2]

The first child of an irradiated mother (1926) to marry did so at the age of twenty in 1946. She has given birth to 2 children, a son born in 1948, now ten years of age, and a daughter born in 1950, now eight years old. Both of these children are normal physically and mentally. The ages of the 45 grandchildren are as follows:

Boys
- Up to 1 year old 2
- 2 years old 5
- 3 years old 4
- 4 years old 2
- 5 years old 2
- 6 years old 5
- 7 years old 2
- 8 years old 2
- 10 years old 1

Girls
- 1 year old 8
- 2 years old 3
- 3 years old 3

[2] Since this paper was presented, 3 additional grandchildren have been born.

4 years old	1
5 years old	1
6 years old	1
7 years old	2
8 years old	1

All these grandchildren of irradiated women are physically and mentally well.

The following illustrations show some of the achievements following irradiation for female sterility.

Mrs. M. M., aged 21, treated in 1927, bore 4 normal children. A son, born in 1921, married in 1949 and sired 2 children, a boy in 1950 and a girl in 1951. A daughter, born in 1930, married in 1952 has 3 children: twins (boy and girl) born in 1952 and a girl in 1958. A daughter, born in 1934, married in 1952 and bore a girl in 1958. A daughter, born in 1940, is not yet married.

Mrs. L. S., aged 33, treated in 1925, bore 3 normal children. A daughter, born in 1928, married in 1949 and bore a girl in 1951 and a boy in 1952. A son, born in 1926, married in 1956 and sired a girl in 1957. A second son, born in 1930, is not married.

Mrs. M. B., aged 22, treated in 1925, bore 2 normal children. A girl, born in 1926, married in 1947, bore three boys, in 1950, 1953, and 1956. A son, born in 1928, married in 1954 and sired a girl born in 1955.

Mrs. I. G., aged 30, treated in 1926, bore 3 normal children. One of twin daughters born in 1927 married in 1951 and bore a boy in 1955 and a girl in 1957. The other twin, married in 1958, as yet has had no children. A son, born in 1930, married in 1954 and sired a boy in 1956.

Mrs. B. B., aged 27, treated in 1947, bore a boy in 1949, a boy in 1952, and a girl in 1955.

Mrs. R. L., aged 24, treated in 1942, bore a girl in 1943, a boy in 1945, and a second boy in 1953.

Mrs. D. F., aged 22, treated in 1949, bore a girl in 1951, a girl in 1952, and a boy in 1954.

Mrs. J. G., aged 32, treated in 1946, bore a girl in 1947 and a boy in 1949.

It is not practicable to reproduce here the many pictures I have, illustrating the normalcy of children and grandchildren of the women treated over the past thirty-three years.

MALIGNANT DISEASE

In only 1 case has malignant disease followed irradiation of a sterile woman.

Mrs. S. C., aged 26, was treated in 1948, failed to conceive, and died Feb. 6, 1949, from leukemia. Since it was not customary to obtain a blood count on patients referred for x-ray therapy for sterility, it is not known whether this patient already had leukemia at the time of irradiation.

There has been no cancer or leukemia of any type noted in any of the children or grandchildren of the irradiated women over the course of the past thirty-three years. Some of these children are now past thirty years of age.

Tables I and II give an overall summary of the results achieved by irradiation for female sterility.

CONCLUSIONS

1. Despite pronouncements of geneticists and physicists that, with respect to genetic damage, there is no safe dose of irradiation, no increase in genetic damage was found in 644 married women given approximately 65 r to the ovaries and followed for one to thirty-three years.

2. The incidence of genetic damage to the children and grandchildren of this group is less than that in the normal population.

3. Some have stated that the series studied is too small to yield significant data. This may be true, but to the author the results are more impressive than the geneticists' calculations based on theory.

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(*For Discussion of this paper, see page 528*)

(*Pro le summario in interlingua, vider le pagina 533*)

A Geneticist Looks at the Radiation Hazard[1]

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TO STATE BEFORE a radiological society that one of the more pressing challenges facing human biologists today is the adequate appraisal of the somatic and genetic hazards posed by our increasing exposure to ionizing radiations has many of the elements of "carrying coals to Newcastle." The radiologist has been keenly aware for some time of the somatic damage to his patients and to himself stemming from x-irradiation. Mute testimony to these dangers is to be found in the book *American Martyrs to Science through Roentgen Rays*. There has also been an awareness, on the part of radiologists, of the potential genetic damage accruing from diagnostic and therapeutic irradiation. This, however, has often been vague and ill defined. The reasons are to be found, I believe, in the general orientation of medicine toward individuals rather than populations. Thus, the radiologist is inclined to justify the use of x-rays solely in terms of the benefits for a specific patient.

The geneticist, on the other hand, tends to think in terms of populations, or pools of genes, and, as a consequence, he may view as suspect a procedure which, while altering the individual risk by only an infinitesimal amount, may effect substantial damage at the population level solely because of the large number of individuals at risk. Unfortunately, this difference in orientation has led to misunderstanding. Thus, some geneticists are apt to view radiologists as, perhaps, callous and unthinking in the practice of their specialty, and some radiologists are tempted to dismiss the geneticist's point of view with the assertion that he is making a mountain of a mole-hill, or that, since the genetic argument is based on the fruit fly—and man is obviously not a fruit fly—the argument has no substance when one speaks of risks to mankind. Fortunately, both of these extreme points of view are on the decline. It is the purpose of this presentation, if possible, to accelerate that decline and to attempt to set in better perspective the problem before us.

The genetic story begins in the third decade of this century with the demonstration by H. J. Muller (1927) that the rate of gene mutation in *Drosophila melanogaster* was increased by exposure to ionizing radiation, specifically x-rays. Through the continuing efforts of Professor Muller and a host of other investigators (Timoféeff-Ressovsky, 1937; Muller, 1954; Russell, 1954), this finding was confirmed and extended to a wide variety of infrahuman forms ranging from bacteria to the mouse. Collectively, the plant and animal experimentation points to certain radiogenetic principles. Chief among these are: The yield in gene mutations is linearly related to dose, and it is independent of the intensity of the exposure; that is to say, the effects of repeated exposure are cumulative. The experimental evidence for linearity rests largely on moderate to high doses (25 r and up) but is sufficiently extensive within this range that geneticists accept, in general, the point of view that "there is no known threshold of radiation exposure below which genetic damage does not occur" (UN Document A/3838, p. 31). The second principle, the independence of yield and intensity of exposure, has recently been challenged. In the mouse, Russell *et al.* (1958) find significantly fewer mutations arising from chronic low-level gamma exposures (to Ce^{137}) than from comparable total doses of acute x-irradiation. It is important to note, however, that the Russells' data on chronic low levels of exposure appear, as they point out, to exhibit a linear relationship between total dose and yield in mutations. Moreover, the difference between the mouse

[1] From the Department of Human Genetics, University of Michigan. Presented as part of a Symposium on Radiation Hazards at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

data and the principle previously given is not necessarily a contradiction, as would appear at first glance. The intensity effect in the mouse is demonstrable only when one measures the number of mutations recovered from gametes derived from exposed spermatogonial cells. No intensity effect is observed in the mouse when one measures the number of mutations recovered from gametes derived from cells exposed at some stage between sperm and spermatocyte. The *Drosophila* data on which the notion of the independence of yield and intensity is based are from experiments of the latter variety, namely, instances where exposure involved cells in some stage of spermatogenesis. The intensity effect in the mouse rests, then, on a type of data not presently available for *Drosophila*. Be this as it may, this apparent dependence in the mouse, and hence possibly in man, of yield of mutations on intensity of exposure does not necessarily alter the basic problem, although, if true, it would necessitate reevaluation of our notions as to the magnitude of the risk.

An appraisal of the potential damage done a human population by exposure to a given dose of radiation involves many unknowns regardless of whether intensity of exposure is or is not a factor to be reckoned with. Our efforts to evaluate the human risk are hampered by the paucity of data on man with respect to such items of basic importance as spontaneous rates of mutation, selection pressures, average overdominance of nominally recessive genes, etc. Moreover, the number of human populations which have sustained appreciable exposures are few, and hence the opportunities to measure directly the genetic damage are limited. Clearly we are confronted with a difficult situation, and one which is aggravated by the necessity of dictating certain "permissible doses." To this point we shall return in a moment, but first let us consider the evidence with regard to the sorts of exposure sustained in a thirty-year period by the "average" individual in the United States.

The ionizing radiation to which we are or may be subject stems from four sources; namely, (*a*) background, (*b*) the fall-out from weapons-testing, (*c*) the use in medicine of x-radiation and radioactive isotopes, and, for a smaller segment of the population, (*d*) occupational hazards. We shall ignore the last in this presentation and focus our attention on the first three. We shall give exposures in terms of radiation experienced in thirty years. This would be the exposure accumulated to approximately the midpoint of the reproductive span.

Background Radiation: Radiation from natural sources is referable to cosmic rays of extraterrestrial origin and to the occurrence in the environment of naturally radioactive isotopes. With regard to the former, the figure 28 mrad/year is frequently used as a mean value for cosmic ray exposure near sea level; this would be a thirty-year dose of 0.84 rads. The value would change, of course, with altitude and increasing geomagnetic latitude.

Radiation from naturally occurring radioactive isotopes arises from exposure to ambient emanations or from the ingestion and deposition of certain of these isotopes in the body. Exposure to environmental radiation will clearly be a function of the amount of radioactive material in the earth's crust at a given place, and this may vary substantially. External gamma radiation out-of-doors has been estimated to vary from 1.5 to 4.8 rads in thirty years in the United States, with most of the population sustaining exposures nearer the former figure. These values are similar to those obtaining in most of Europe but appreciably lower than the exposures experienced by some individuals. In the Chavara-Neendakara area of Kerala (India) and the Manavalakurichi region of Madras State doses of external gamma radiation inside dwellings may run as high as 45 rads in a thirty-year period.

While our knowledge regarding exposures from ingested radioactive isotopes is far from complete, it would seem safe to assert that among the naturally occurring isotopes, the most important are C^{14}, K^{40}, and Ra^{226}. Though there are differences in the sites of

deposition of these substances in the body, *e.g.*, Ra^{226} is selectively incorporated into bone, whereas C^{14} is not, the total thirty-year dose to the gonads would appear to approximate 0.6 to 0.7 rads. This figure may vary considerably, however, with diet and water supply.

Fall-out from Weapons-Testing: The concern over fall-out rests on the increase in external gamma irradiation which it may occasion, and on the increase in body burden from the ingestion or inhalation of fission products, residual fissionable material, and neutron-induced radioisotopes. Estimation of the dose of radiation from these sources involves many unknowns. It has been estimated, however, that the gonad dose, assuming weapons-testing continues at the present rate, will be of the order of 0.10 mrem in thirty years. Of this, 20 to 40 per cent will be derived from external sources. Principal concern is with the behavior of Sr^{90} and Ce^{137}, both of which have long half-lives and tend to be selectively incorporated into bone. They may, therefore, be of more importance with reference to the frequency of leukemia than in relation to mutations arising in the germ line.

Medical Use of Ionizing Radiation: The most extensive body of data yet published bearing on the medical use of ionizing radiations is to be found in the Report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UN Document A/3838). Available data suggest that the thirty-year gonad dose in the United States is not less than 1.5 rad, with 4.5 rad being the probable value. It is of interest that diagnostic uses make a much larger contribution to this total than do therapeutic uses, and that six or seven types of examination account for some 85 per cent of the diagnostic dose. These procedures, which constitute less than 10 per cent of all x-ray examinations, involve the pelvis and lower abdomen, where the gonads are in the primary beam. We have much to learn, however, before this source of radiation can be more precisely evaluated. At present, data are particularly scarce with regard to (*a*) the use of x-rays by nonradiologists, (*b*) the exposures sustained in roentgen treatment, and (*c*) the diagnostic and therapeutic use of internally administered radioisotopes. In addition, we have less than the desired amount of information on the expected future number of children of an individual of age x receiving irradiation either diagnostically or therapeutically. The importance of this latter information to the geneticist need hardly be stressed.

It has been asserted that the figures just cited for the medical use of roentgen rays, while applicable when these data were collected by Laughlin and his co-workers (1957), are higher than would now be true by, perhaps, a factor of 2. Personally, I would doubt this. Unquestionably there has been a movement toward eliminating unnecessary exposures, and toward reducing the radiation dose through the use of faster films and rectangular ports. This trend is most pronounced in the major medical centers of the country, but it is debatable whether much headway has been made in the average hospital where, after all, a very sizable portion of our population receives the bulk of their exposures.

Before we turn to the data on the genetic hazards to man following exposure to ionizing radiations, let us summarize the information with reference to "average" exposures in the United States. From the three common sources, we find that the thirty-year dose lies in the neighborhood of 7 to 8 rads, with medical use of ionizing radiation accounting for over half of this amount. The actual distribution of exposures must, however, be markedly skewed to the right.

DATA ON GENETIC HAZARDS

As we have indicated, the data available on human populations for appraising the genetic hazards are scanty. Thus far, only six studies have been published. These are the investigations of Macht and Lawrence (1955) and Crow (1955) on American radiologists, the work of Turpin, Lejeune, and Rethore (1956) on French men and women receiving sizable therapeutic exposures, the study of Tanaka and Ohkura (1958) on Japanese x-ray technicians, Kaplan's

(1959) follow-up of women treated for sterility by x-irradiation,[2] and the reports on the survivors of the atomic bombings of Hiroshima and Nagasaki (Neel and Schull, 1956; Schull and Neel, 1958, and in press). At least two other studies are in progress or contemplated, one in Brazil on radiologists and the other in India on the inhabitants of the monazite sands of Kerala and Madras State. In the six studies cited, observations on a variety of attributes of the newborn have been made, including sex, occurrence of malformation, mortality, birth weight, and certain anthropometric measurements indicative of general growth.

The observations on mortality, birth weight, and anthropometry may be summarized rather easily. None of the studies has reported significant differences between exposed and nonexposed populations with respect to these variables. The situation regarding congenital malformations is somewhat more complex. Neither Kaplan nor Neel and Schull demonstrate differences in the frequency of congenital malformations among the offspring of exposed and nonexposed parents. Macht and Lawrence, on the other hand, report a higher frequency of abnormalities among the offspring of radiologists than among the children of individuals in other medical specialties. For several reasons we are reluctant to accept this difference as real. First, the difference observed is due largely to two diagnoses, namely, congenital heart disease and hemolytic disease of the newborn. With regard to the former, no differences among the various exposure classes in Hiroshima and Nagasaki were found. The increased incidence of hemolytic disease of the newborn is difficult to interpret. Macht and Lawrence score children born to radiologists prior to their entry into their specialty as "control," and we know that hemolytic disease of the newborn is a disease of later-born children. Thus the scoring procedure would tend to enhance any difference which might in fact be present. A second difficulty with this study is that the data suggest that at death the children of radiologists are more apt to be autopsied than are the children of nonradiologists. It is well known that postmortem study will reveal more congenital anomalies than are apparent on clinical examination alone. In view of these objections, it would seem appropriate to take the position that no increase in congenital malformations following parental exposure has yet been demonstrated.

The one finding which seems to emerge from the various studies has to do with the sex ratio. You will recall that sex determination in man is a chromosomal phenomenon, the male having dissimilar sex chromosomes whereas the female has similar ones. The chromosome unique to the male we designate as Y, and the one common to males and females as X. The Y-chromosome appears to be relatively inert, genetically speaking, and we shall therefore focus our attention on the X-chromosome. Now if one were to irradiate males, and if mutations were induced in the male X-chromosome, these mutant genes would be transmitted only to the daughters of the irradiated males. If these mutants were incompatible with life, that is, if they were lethal, then we would expect a reduction in the number of female infants born to exposed fathers. This reduction would be due primarily to sex-linked dominant lethals, although one might anticipate the manifestations of some recessive lethals because of the fortuitous combination of an induced mutant and a similar gene already present in the population. If females were irradiated, one would be exposing, in a sense, only X-chromosomes. These X-chromosomes would be randomly distributed among the sons and daughters of the exposed mothers. If lethal mutants were induced, they would more frequently find expression in the male, since he has only one X-chromosome and a recessive mutant therefore could not be covered, so to speak, by a "normal" gene. To recapitulate, if fathers were exposed, we would expect a reduction in the number of females, or a relative increase in the proportion of male births. If mothers were exposed, we would

[2] See p. 518.

expect a reduction in the number of males, and hence in the proportion of male births. If both parents were exposed, we might expect the maternal and paternal effects to be additive though not necessarily equal.

We ask now what is observed in the five studies reporting data on the sex ratio? (*a*) Macht and Lawrence find that the sex ratios among births to radiologists and to nonradiologists do not differ significantly; however, the observed difference is one of fewer males among the children of radiologists. This is contrary to the genetic hypothesis.

(*b*) Kaplan finds 281 males and 284 females among 565 children of previously irradiated mothers where the sex of the offspring is known. We would expect some 291 males if the sex ratio among these children was the same as that obtained in the general population of infants in the United States. This difference between the general population sex ratio and that obtaining in Kaplan's data is not statistically significant, but the observed difference is in the direction of the genetic hypothesis. It should be recognized, however, that the general population of the United States may not be a valid control in this instance.

(*c*) Tanaka and Ohkura report a sex ratio of 0.5525 among the offspring of radiological technicians as contrasted with 0.5259 among the offspring of pharmacy technicians. While these two figures are both higher than the average for Japan (0.5124), the difference between the groups is significant, and in the direction specified by the genetic hypothesis.

(*d*) Turpin, Lejeune, and Rethore studied one group of females and three groups of males. Among the latter were 368 cases where the radiation was delivered high up in the lumbar region or to the thigh, 180 cases where radiation was to the pelvic area but the gonads were probably shielded, and 786 cases where the subjects were irradiated in the pelvic region under conditions making protection of the gonads impossible. These authors give the sex of the children born to the second and third groups of males, but not the first. In the analysis of their data, they reject the second group because of the uncertainty surrounding the exposures in this group. We shall not reject this group for our calculations, since it is certain that some radiation was delivered to the gonads, and the actual dose is not critical to our argument. Turpin *et al.* compare the sex ratio before exposure with that following exposure. Three comparisons are possible. In two instances the exposed parent is the father, and in one case the exposed parent is the mother. Of these three comparisons, two are in keeping with the genetic hypothesis and one is not. Thus our box score, at this stage, is 4 for and 2 against the model.

(*e*) The largest body of data comes from Japan. Here, when one takes into account the method of data collection and the biological relationship between the parents, it is possible to generate 12 regression coefficients relating the change in the sex ratio to estimated parental exposure. Of these 12 coefficients, not less than 10 have the sign which one would expect on genetic grounds. If, then, we utilize all of the observations on the sex ratio, we find that 14 out of a possible 18 are in keeping with genetic theory. Now the probability of observing this array if the signs were equiprobable is less than 2 chances in 100. Of equal interest is the fact that, for those studies where parental exposure can be quantified, the regression coefficients are surprisingly similar, about 0.0060/100 reps (or r). In terms of the frequency of induced sex-linked lethal mutants, this implies a value of about 2.4 per cent per 100 reps. The corresponding value in *Drosophila* is 3 per cent per 1,000 r. From these calculations, man would appear to be one order of magnitude more sensitive to irradiation than *Drosophila*. It is interesting to note, in this connection, that the evidence on induced specific-locus mutants in the mouse suggests a value ten times greater than in *Drosophila*, or a value of the same magnitude as that here implied for man.

Does this, then, mean that a genetic effect has been demonstrated? Conclusively, no! The sex ratio, despite the nicety of

the genetic argument, varies in strange and inexplicable ways. Moreover, in arriving at this statistic we have, as will have been noticed, assigned equal weight to all of the investigations. Yet only one of these studies was prospectively oriented and had each observation confirmed by a physician. The retrospective studies were almost without exception questionnaire surveys, the biases and pitfalls of which are well known. Thus, we are in the somewhat anomalous position of observing an effect consistent with genetic notions, but feeling reluctant to assert that the results *must* be due to the operation of sex-linked lethal mutants.

DISCUSSION

Let us return now to the genetic risks to mankind from ionizing radiations. You will all have seen extravagant statements regarding fall-out and congenital malformations, or fall-out and leukemia—statements which can in no way be rigorously defended. While computations of this variety may and do have value to the geneticist as a guide to his thinking, publication of these "guesstimates," even with all of the necessary restrictions, can serve only to confuse, since persons outside the realm of science are, in general, not used to weighing and evaluating uncertainties. All too often pronouncements of the variety to which we have referred have the mantle of science but are in reality expressions of value or political leaning.

We do our science a tremendous disservice when, directly or indirectly, we permit judgments on fact to be confused with facts. This distinction, however, is not always easily maintained. A case in point is the matter of "permissible doses." The very name suggests that such an exposure is without harm, whereas the genetic evidence would indicate that no dose is too small to induce mutations; in a sense, then, no exposure is permissible. "Permissible doses" are obviously judgments on facts, representing an effort to equate the potential benefits from the uses of ionizing radiation with the possible damage it may produce. Unfortunately, neither side of this equation can be assayed reliably, and there has been a preoccupation on the part of the press (see WHO Technical Report Series, 151) with the dangers rather than the benefits of ionizing radiation. An undesirable by-product of this unbalanced approach may be public apathy or denial of the risks, on the one hand, or, on the other, an effort by the laity to pass judgment on the necessity of each and every roentgenogram which may be ordered. This usurpation of the prerogative which the physician has always viewed as his own—and rightly so—does not contribute to the rapport between patient and physician so essential to the proper practice of medicine.

While it is obviously imperative that the public be informed of the radiation hazard, it seems to me equally important that it be understood that exposure to ionizing radiation is but one of a number of dysgenic forces at work. Certainly the tremendous social upheaval of the last century and the advances of medicine have exerted and are exerting pronounced effects on man's genetic make-up. No one advocates a return to the medicine of a half century ago, or to a relatively immobile, primarily agrarian society such as preceded the industrial revolution. There are those, however, who would turn back some of the advances of modern physics, justifying themselves on genetic grounds. I am not pleading that we ignore the radiation hazard—far from it—but I am pleading for perspective and the realization that we must learn to live with this new risk. We could more profitably spend our time deciding how best to meet this challenge and to secure the information which we need for its appraisal rather than continuing to dwell on the less happy aspects of the problem. Bluntly stated, we could do with somewhat more work and fewer speculations.

From what has been said, it should be clear that recommendations in the light of our present knowledge cannot be especially precise. But certainly until such time as more information is available, wisdom would dictate a conservative approach.

wherein we would limit our exposure as much as is consistent with the practice of good medicine.

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(*Pro le summario in interlingua, vider le pagina 534*)

DISCUSSION

(Papers by Hodges; Powell; Webster; Snegireff; Kaplan; Schull)

Robert S. Stone, M.D. (San Francisco, Calif.): I shall limit my discussion to three of these tremendously interesting papers. May I say a word of thanks to all the authors *en masse* rather than repeating it for each paper.

I would like to discuss first Dr. Powell's paper in connection with government investigation of radiation hazards in doctors' offices. I will limit myself largely to one point: I think that the government will have to set up regulations for the installation and operation of x-ray machines. It should never regulate the practice of radiology any more than it should the practice of any part of medicine or surgery. However, we all know that, regardless of whether everyone in this room observes all the safety factors that have been discussed today, the number of roentgen examinations with machines operated contrariwise is still in the tens of thousands.

A nurse called me recently to tell me that she was disturbed because, just after having started to work for a nose and throat specialist, the first thing he taught her was how to take roentgenograms of the spine. She was also worried about the small size of the room which contained the x-ray apparatus, necessitating that she stand in the hall while the examination was done. That is an example of installations that exist all across the country.

I don't know how we are going to correct the situation except to ask the government to establish and enforce safety regulations.

Dr. Schull has presented a very interesting discussion of radiation effects from the geneticist's point of view. He has ruled invalid most of the evidence advanced as demonstrating irradiation effects in man. He showed quite clearly the mechanism by which the sex ratio could be affected by irradiation but he apparently doubts even such changes in sex ratio as have been demonstrated. However, he has taught us an important lesson—the difference in the point of view of the geneticist and the radiologist. He has pointed out that the geneticist thinks in terms of the population as a pool of genes, whereas we think in terms of our single patient. It is difficult for either group to appreciate the other's point of view.

I have made the statement, while talking to groups living at sea level, that they need not fear a chest roentgen examination, since 300 such examinations during one year could be made, with the genetic dose still not as great as that received each year by people living in Denver. The geneticist, however, is not interested in whether people living on the coast get as much radiation as those in Denver, but in how to lower as far as possible the radiation level of the population of the whole world.

In connection with the use of a permissible dose, the practical problem is that, because radiations have been and will continue to be of great benefit to mankind, they will continue to be used. Nuclear reactors will be necessary as sources of power in the future and they will add more radiation hazards. People will of necessity be irradiated and rules on

what is permissible must be established. Only time will tell whether our best guesses are correct, but we do need a quantity of radiation that we say is "permissible" to the best of our knowledge at any given time.

Regarding Dr. Kaplan's paper, I think it is interesting that he is not claiming that geneticists are wrong and that the records of child-bearing in several hundred women he treated have not proved or disproved any genetic theory. By presenting this material he is doing a great service both to our patients and to ourselves, because it convinces us, and the laity also, that women can be exposed to radiation to the extent reported and still have normal children. We have all received inquiries from patients who have a guilt complex because they bear children after radiation exposures. They wonder if they have inflicted a terrible injustice on the child. I think this guilt complex will become an important factor with which to deal if we cannot counteract some of the publicity of the past. Dr. Kaplan's paper indicates that, so far as individuals are concerned, we need not expect to detect any changes as a result of the fact that a few women received radiation treatment to their ovaries. The difficult point for us to convey to the public is the difference between immediate effects on first and second generations of a few people, and the long term genetic effects on the population as a whole.

This report of Dr. Kaplan's is a documentation of the largest and best studied group of women treated for sterility with a method that we all hope will be abandoned.

Wendell G. Scott, M.D. (St. Louis, Mo.): Dr. Hodges has given us a splendid summary of practical methods of how to minimize radiation dosage in our daily practice. I agree with everything he said.

The paper by Dr. Powell, "The Government looks at Radiation Hazards," impressed me as a sane and sound approach to this problem, based, as it is, on the mutual understanding and co-operation of physicians, our national scientific organizations, and the Public Health Service. As Dr. Powell mentioned, the right and duty of the practitioner to determine what is best for the patient must be preserved.

The registration of all x-ray-producing units would be of no avail without the implied threat that this can mean inspection and survey evaluation. The objective is laudable and Dr. Stone's remarks lend it emphasis, but I bristle a little at the thought of a government inspector coming into my department or office. I would not have the same reaction were it someone from an accredited board of inspection such as now exists for approval of residency training in hospitals. Such an inspection program represents a very sizable effort and would require a large staff of trained radiation monitors or technicians that have first to be developed—a task which I understand the U. S. Public Health Service is prepared to undertake.

I was pleased to hear Dr. Powell state that any attempt to control clinical procedures by legislation or inspection is destined for failure, for I am certain the medical profession would not tolerate it. The profession would, on the other hand, welcome assistance in the enforcement of standards of practice established with our guidance and in the disposal of obsolescent equipment.

The paper by Edward Webster, "The Physicist Looks at Radiation Hazards," introduces a fascinating and refreshing point of view. He has attempted to reduce all the complicated problems, including the patient-physician relationship and the exercising of clinical judgment in the handling of patients, to a mathematical formula—a point of view which is thought-provoking and interesting. I am not qualified to discuss Dr. Webster's mathematical procedures, but they sounded reasonable to me.

I object, however, first of all, to the use of the study by Court-Brown and Doll on the induction of leukemia following irradiation for ankylosing spondylitis for comparison with results that might follow diagnostic examinations, which deliver a much smaller bone-marrow dose. I object also because the doses employed in England and Holland were much larger than those prescribed in this country. Furthermore, this practice never became widely accepted in America and has now been almost abandoned. I do not like to have the impression created that this type of treatment is still going on to any extent.

I take the same stand on the inclusion of results reported by Simpson and Hempelmann on the induction of cancer after radiation treatments to the thymus in children. This again is an obsolete practice—one that has been discarded and no longer offers a major threat.

The study by Stewart, which attempted to relate fetal exposure to an increased incidence of leukemia is open to serious question. As Burnet[1] says, and I quote: "I felt almost convinced that pelvic x-rays in pregnancy was the factor. It seems to fit all the requirements except the completely decisive finding that at least 85 per cent of cases of leukemia in childhood were from pregnancies not exposed to x-rays." Moreover, I doubt if many in this country are doing routine pelvimetric examinations on pregnant women. In fact, I am sure that for some years there has been a very marked decline in the use of this procedure.

What I have been trying to point out is that discarded or obsolete radiotherapeutic and diagnostic practices should not be used in calculating present-day hazards. Such hazards should be analyzed on the basis of present-day procedures and measurements.

[1] Burnet, Sir Macfarlane: The Strange Leukemia Epidemic. Saturday Rev., Aug. 2, 1958, pp. 438–39.

Dr. Webster's method did pick up one weakness, and that is the lack of careful monitoring of the units for mass chest surveys, particularly those that are not under a radiologist's supervision. I am in agreement with his emphasis on fast screen-film combinations and high-kilovoltage technic and have maintained that radiation dosage can be reduced 75 or 85 per cent immediately, but I can't achieve his 99 per cent reduction—a goal worth shooting for. Dr. Webster, as you told me when you gave me your paper, it was provocative.

Dr. Snegireff's paper is a model of a carefully prepared study of an elusive problem. His approach gives you confidence and you feel that whatever he comes up with in his final analysis will be solid. It is a pleasure to know that such a high-grade examination is being carried out in this field, although it should be emphasized, as Dr. Snegireff mentioned, that the procedure of thymic irradiation has been discarded.

About Dr. Kaplan's paper, I really do not feel competent to analyze it properly, for in effect it is really a study on human genetics. His material represents a valuable collection of cases and affords a unique opportunity for a careful appraisal and examination by a geneticist who can evaluate the minor and less obvious genetic implications. I hope that Dr. Kaplan will make accessible this unusual opportunity to a qualified geneticist. He has the opportunity to offer a real service to genetics by letting them review his studies.

I want to reiterate that this method of treating infertility and sterility in women never had more than a very limited acceptance in this country and for some years has not been used by radiologists.

Dr. Schull has a broad understanding of the genetic problem, for he points out that the radiologist views the problem from the individual's standpoint, while the geneticist views it as it affects the whole population. As we better understand each other, we find that our problems are not so far apart, as he has so ably shown us. Continuing to meet and exchange our knowledge, as we have done today, brings us a step closer to a satisfactory solution. The conclusion that wisdom would dictate a conservative approach wherein we would limit our exposure so far as is compatible with the practice of good medicine is the same as ours—that any dose to the gonads is too high if it can be lowered. We have to make efforts every day to become more gonadal conscious and to instruct our technicians to think of gonadal protection every time a film is exposed. We must work hard and constantly to keep exposures to a minimum. It is better to minimize exposure than to minimize warranted examinations.

In the few seconds left, I want to speak about the figure 4.5 rad as being the probable average gonadal dose in the United States. It was suggested from the original survey conducted by Laughlin and Pullman in their study, for the Genetics Committee of the National Academy of Sciences on the Biological Effects of Atomic Radiation. This was presented as a preliminary report, but was never officially released by the National Academy because of objections from various individuals and groups who were afraid that the estimate of 4.6 r ± 3 would be taken and used as a true value. It is not; it is merely an estimate, obtained from data of varying reliability, but it is already widely quoted and one would be led to accept it as a fact. The October 1957 report of the International Commission on Radiologic Protection Units and Measurements, as well as that of the U. N. Scientific Committee on the Effects of Atomic Radiations, April 1957, state that "no records are available detailed enough to use for the proper assessment of the gonadal doses to the population." Laughlin and his associates, in a paper appearing in December 1957, discuss the studies and surveys that would be required for obtaining the necessary information to develop this figure. The one thing we know is that it isn't 4, 5, or 4.6, but possibly ±3, and that at best it is an estimate. New studies in up-to-date departments employing up-to-date technics have resulted in much lower figures. Those by Norwood in Hanford, Washington, indicate an average gonadal dose of 1.4 r.

In developing this figure one will have to take into account not the amount that reaches the gonads in individuals in the reproductive age, but only in those who reproduce after the exposure—another factor that was not considered. Thus, when you see this figure, remember how it was obtained. I have mentioned this only as a plea that we get up to date and use present-day exposures, present-day practices, and present-day procedures.

I want, finally, to refer to the figures which Dr. Schull used when he said that 85 per cent of the total diagnostic gonadal dose arises from seven types of examinations. These come from a survey of the work load at the University of Michigan in Dr. Fred Hodges' Department. These seven types of examination constitute about 10 per cent of all examinations and only half of these are on individuals thirty years of age or younger. In any working day there are only a few such patients, so that extra measures for protection with gonadal shields do not constitute a burden on the staff.

I congratulate Dr. Robbins on a splendid Symposium, for sessions of this caliber, with emphasis on facts and a minimum of emotion, cannot but result in fuller co-operation to bring our problems into better perspective and to aid us in our effort to keep diagnostic radiology safe.

Hymer L. Friedell, M.D. (Cleveland, Ohio): It has been a privilege to listen to these excellent presentations this afternoon. All of the papers were instructive and their discussion pertinent. I came here prepared for almost anything, from a few words to an extensive discourse. I find that a long discourse is completely unnecessary, since so

many things have already been said. In view of the shortness of time, I will confine myself primarily to Dr. Kaplan's paper on the genetic effects of irradiation for infertility and sterility, which I received prior to the meeting and have had a real opportunity to examine.

In the total number of gross abnormalities there appears to be no significant difference between those which are observed in Dr. Kaplan's treated population and those which might be expected from an untreated population. In the first generation, large differences would have to exist to be detectable, in view of the comparatively small number of cases. Therefore, small differences have not been eliminated.

However, I would like to point out some features of the data which, though not immediately obvious, may be significant if they prove to be accurate. I believe the changes observed to represent some type of genetic alteration, but genetic change or not, an unusual observation can be made. On the basis of genetic theory, most mutations are expected to be recessive. Therefore, in the first generation one is unlikely to observe any effect except in those instances where the chromosomes would be unpaired—that is, in the male offspring. It is interesting to note that there were 11 postnatal deaths, all occurring in males. That this should occur by chance is exceedingly unlikely and may be highly significant. Thus a genetic injury has not been ruled out.

However, this is not the entire problem. Even assuming that a genetic injury has occurred, one must always weigh the advantages of increased fertility against the disadvantages associated with genetic risk. It is conceivable that one might argue that an increase of fertility of 60 per cent in previously infertile women is an important advantage, and it is conceivable that it might be possible to argue that this outweighs the hazard. It would also be necessary to show that other methods are less efficacious than x-ray therapy. In this respect I have made inquiry into our own maternal health records, and it is interesting to note that we have a 60 per cent improvement of fertility after various therapeutic measures, none of which includes radiation. I agree with Dr. Stone that in view of other methods of treating fertility it is time to consider abandonment of radiation for this purpose.

I would like to turn for a moment to Dr. Schull's discussion. I thought it very clear and lucid, and it covered the subject for the radiologist very well. There is one element, however, that I think is the heart and soul of determining genetic damage at very low radiation levels. I do not believe there is any doubt that genetic effects occur at high doses, and the question is really one of deciding what occurs at very low doses. If one had the mechanism clearly in hand, one might speak confidently, but since there are many hiatuses in our information, there has been considerable recourse to the dose response curves. Very briefly, a dose response curve which is linear (really exponential) may be considered to be a single event function. Under such circumstances, there is no threshold and the response is completely cumulative. If a nonlinear type of curve is obtained, however, it is incompletely cumulative and there is a very strong possibility that a threshold may exist. Therefore, if one is going to use the dose response curve, it is necessary to examine this as thoroughly as possible. One of the best tests of the dose response curve is to compare the fractionated or fragmented dose at some point on the curve with the unfractionated dose. In the single-event type of curve, the effects would be exactly equal. In the multiple-event type of curve, or other nonlinear type of curve, the effect of the fractionated dose will be considerably less than that of the unfractionated dose. Another way of putting it—low intensities will give much lower effects than high intensities. It is interesting to note that recent work by Russell has shown a marked difference in effects in mice between high intensity and low intensity. At the very least, this means that there is probably incomplete additivity and the effects are not dose-rate independent. It could even mean that an actual threshold might exist.

SUMMARIOS IN INTERLINGUA: HASARDOS DEL RADIATION

Observationes De Un Radiologo Con Respecto Al Hasardos Del Radiation

(*Pagina 481*)

Il ha non essite demonstrate e, in le opinion del autor, va nunquam esser demonstrate que le micrissime histodoses que es applicate in appropriatemente conducite studios roentgenologic augmenta le tendentia mutatori o le incidentia de leucemia o reduce le superviventia del individuo, sed il existe omne ration pro creder que tal effectos es producite in humanos e animales laboratorial per doses plus forte. Per consequente, omne precaution practic debe esser prendite pro tener le histodoses applicate in examines roentgenologic al minimo possibile.

Examines innecessari debe esser evitate. Fluoroscopia debe esser usate solmente quando illo es indispensabile. Quando on filma le pelve, le vias urinari, o non importa qual altere parte resultante in que le testes jace directemente in le fasce, illos debe esser protegite. Un kilovoltage de 90 o 100 e un filtro de al minus 2 mm es adequate pro objectivos diagnostic e debe esser preferite al uso plus conventional de 70 kv con un filtro de 0,5 mm proque illos reduce le histodosage per circa 50 pro cento. Films e radioscopios rapide con le correcte exposition e un disveloppamento complete debe esser empleate. Le film debe reciper le exposition minimal sufficiente pro le disveloppamento complete in solutiones de concentration e temperatura standard. Tal expositiones se face le melio con photochronometros, e le processage es complite le melio in dispositivos automatic.

Fenestras rectangular (plus tosto que circular) reduce le radiation inutile ab le nivello de 75 pro cento del fasce utile usque a 13,4 pro cento in le caso de films de 14 per 17 pollices, ab 80 usque a 19,2 pro cento in le caso de films de 10 per 12 pollices, e ab 87 usque a 23,75 pro cento in le caso de films de 8 per 10 pollices. Le uso de micre fenestras rectangular es considerate como specialmente importante in fluoroscopia e films a objectivo circumscripte.

Le Puncto De Vista Del Governamento Relative Al Hasardos Del Radiation

(*Pagina 489*)

Si le problema del hasardos de radiation debe esser attaccate rationabile- e appropriatemente, un precondition essential es le cooperation mutual inter le practico individual, su organisationes, e le agentias del governamento. Le preste cooperation e le active participation de radiologos in le programmas del agentias governamental es un del melior methodos pro assecurar que nulle mal-orientate e mal-considerate action es initiate.

Le governamento de su parte pote esser de adjuta per supportar le recerca medical, per contribuer al education del publico, per mantener le equipamento in le plus salve condition de functionamento, e per provider un base legal pro le exclusion de mal-preparate e incompetente individuos ab le manipulation de un potentialmente hasardose apparatura. Precisemente como al tempore presente agentias official assiste in imponer altere standards establite per le professiones ingagiate in le practica general del artes iatric, assi on pote etiam supponer que illos va monstrar se preste a assister in le imposition de standards que provide un protection contra le hasardos del irradiation.

Le Hasardos Del Radiologia Diagnostic: Le Puncto de Vista De Un Physico

(*Pagina 89*)

Mesmo si le standards le plus pessimista es applicate, le hasardos presente pro le patiente in le radiographia diagnostic es micre. Illos es satis micre pro esser plus que compensate per le expectation de un micre beneficio potential pro le patiente. Le hasardos genetic, que es un pauco plus grave in le majoritate de tal examines, es ultrapassate per le hasardos de portar continuemente un horologio bracialetto con quadrante a radium o, apparentemente, per le hasardo create per le augmentate temperatura del gonades que es un effecto de nostre portar pantalones. In le caso de roentgeno-examines thoracic in massa, un comparation del beneficio e del noxia es theoricamente possibile. Un consideration preliminari indica un grande balancia de beneficio si ben-conate roentgeno-apparaturas es usate.

Grande reductiones del dose es technicamente possibile per varie methodos, notabilemente le uso de augmentate kilovoltages e de plus moderne e rapide combinationes de film e radioscopio. Per iste medios insimul, reductiones per un factor de 100

pote esser obtenite in comparation con le nivellos que es currentemente usual, ben que le complete realisation de iste objectivo depende possibilemente del disveloppamento de scopios a emission verde con alte numero atomic. Le costo a pagar pro tal reductiones es un marcate perdita de detalio e de contrasto. Le radiologo debe determinar le circumstantias sub le quales il es justificate sacrificar le qualitate del radiogramma in le interesse de un hasardo reducite.

Le Elusivitate De Neoplasia Post Roentgeno-Therapia Pro Allargamento Thymic In Patientes Pediatric

(*Pagina 508*)

Es presentate un reporto preliminari relative a un effortio de determinar le incidentia de formationes neoplastic post roentgeno-therapia pro allargamento del thymo in juveniles.

Un studio post-tractamental esseva effectuate con 333 subjectos qui consultava le departimento de patientes visitante de un sol institution a causa de tonsillas allargate e de repetite infectiones ocular, aural, nasal, e gurgital durante le annos de 1923 a 1947. Le hospital in question habeva un uniforme methodo de roentgeno-tractamento pro allargamento de glandula thymic, instituite in 1926 e continuate durante plus que duo decennios.

Ex le serie de 333 patientes, 148 habeva recipite roentgeno-irradiation pro allargamento thymic de infantia o pueritia, 23 habeva non-tractate allargamento thymic, e 162 habeva nulle detegibile allargamento de ille glandula. Al tempore del presente reporto nulle morbo maligne esseva trovate in ulle del 148 subjectos tractate pro allargamento del glandula thymic, ben que 75 habeva essite sub observation durante plus que vinti annos. In 2 patientes, benigne conditiones thyroide se habeva disveloppate. In le un il se tractava de un adenoma, in le altere de un morbo cystic. Tres patientes moriva ab morbos nonmaligne. Le gruppo de controlo de 162 subjectos esseva etiam sin cancere. In iste gruppo, 6 mortes occurreva, omnes in consequentia de morbos nonmaligne. Le previemente reportate alte incidentia de cancere primari del thyroide e de leucemia post irradiation thymic non es corroborate per iste investigation.

Le observationes del autor esseva supportate per un serie inedite de casos vidite in un altere institution del mesme region.

Le factores que explica le differentias inter iste e previe series include variabiles como le etate del subjectos al tempore del roentgeno-therapia, le dose total, le intervallo inter doses multiple, le duration e le completessa del observationes, le sexo del patientes[5], le tempore total del observationes post-therapeutic, le selection del gruppos de controlo o de comparation ab areas geographic particular, le probabilitate de cancere in un sito primari particular, e possibilemente factores de stato economic.

Ante que conclusiones definitive pote esser formulate, il es necessari instituer un registration systematic e le complete observation post-tractamental de omne patientes exponite a doses therapeutic de radiation ionisante pro conditiones altere que morbo maligne. Le observationes post-tractamental deberea, idealmente, esser continuate durante le integre vita de omne patiente.

Effectos Genetic In Filios E Granfilios De Feminas Tractate Pro Infertilitate E Sterilitate Per Therapia A Radios X: Reporto De Un Studio De Trenta-Tres Annos

(*Pagina 518*)

In le curso del passate trenta-tres annos, 800 feminas esseva tractate per le autor pro sterilitate per medio de therapia a radios X. Sex centos quaranta-quatro de illas esseva observate durante periodos de inter un e trenta-tres annos. Duo centos

novanta-tres non concipeva; 351 habeva 688 pregnantias; e 318 parturiva 566 infantes (282 mascule e 284 feminin). Iste total include 543 san e normal infantes vive, 260 pueros e 283 pueras. Trenta-cinque de iste pueras ha parturite 45 graninfantes del quales solmente 1 ha morite (per toxemia eclamptic del matre). Le procentage de parto immatur in iste gruppo irradiate es 17,7; de morte fetal 20,6; de morte-nate 1,4; de anormalitate cognoscite 1. In normales, iste magnitudes es, respectivemente, 10+; 16,6; 4; 4,2 a 7. Durante que le proportion inter le sexos es 50 a 50 in normales, in le presente serie illo esseva 50,2 a 49,8, con pueras plus numerose que pueros. Le autor conclude que le incidentia de noxia genetic in infantes e graninfantes de feminas tractate pro sterilitate per medio de irradiation es minus que le correspondente incidentia trovate in un population normal.

Un Geneticista Considera Le Hasardos Del Radiation

(*Pagina 522*)

Le radiologo inclina a justificar le uso de radios Roentgen exclusivemente super le base de beneficios pro le specific patiente sub consideration. Le geneticista, del altere latere, tende a pensar con referentias al population total, i.e. a massas de genes, e reguarda como suspecte un methodologia le qual—durante que illo altera le risco individual per solmente un amonta infinitesime—effectua possibilemente un noxia considerabile in le population, si solmente a causa del grande numero de individuos concernite.

Collectivemente, experimentos vegetal e animal suggere certe principios radiogenetic. Le plus importante de illos es: Le rendimento de mutationes genic es relationate linearmente al dose e es independente del intensitate del exposition, i.e. le effectos de expositiones repetite es cumulative.

Le radiation ionisante al qual nos es o pote esser exponite se deriva de quatro fontes: Radio-activitate natural, precipitation post tests de armas atomic, le uso medical de radios Roentgen e de radio-isotopos, e, in le caso de un plus micre segmento del population, hasardos occupational. Ab le prime tres fontes, le dosage tri-decennial in le Statos Unite es in le vicinitate de 7 a 8 rads, e le uso medical de radiation ionisante representa plus que un medietate de iste quantitate.

Il existe in forma publicate sex studios de gruppos de population human que contribue datos al evalutation del hasardos genetic de irradiation ionisante. Iste studios es passate in revista. *Un* constatation que pare emerger ab le massa del datos concerne le proportion sexual in le prole de personas exponite a radiation ionisante. A generalmente parlar, le observationes in re iste puncto supporta le realitate de un effecto genetic, sed—in vista del natura del studios—il pare remaner questionabile si le resultatos *debe* esser debite al mechanismo de mutantes letal a ligation sexual.

Ben que in le lumine del currente informationes il non es possibile arrivar a un evalutation exacte del hasardos de radiation e offerer recommendationes precise pro combatter los, le dictato del sagessa es sin dubita un procedimento conservatori con respecto a iste problema, lo que significa un limitation del expositiones a irradiation ionisante in tanto que isto es compatibile con le practica de bon medicina.

Acromegaly[1]

HOWARD L. STEINBACH, M.D., ROBERT FELDMAN, M.D., and MINNIE B. GOLDBERG, M.D.

ACROMEGALY IS AN insidious disease affecting all the tissues of the body. It progresses so slowly that many years may pass before the victim or his associates become aware of the widespread changes that have occurred in his appearance and health. From its obscure inception, the disease progresses slowly, perhaps intermittently, and ultimately, if not arrested, is capable of producing grotesque appearance, great disability, and sometimes death.

It has been well established by pathological studies of patients and by the experimental production of a similar condition in animals that the disease is due to an increase in size and function of a portion of the anterior lobe of the pituitary gland (12). The lesion of the pituitary is in most cases an eosinophilic adenoma, occasionally a hyperplasia of the eosinophilic cells without adenomatous formation, or rarely a chromophobe adenoma or eosinophilic adenocarcinoma.

The symptoms and signs are the result of three processes: the expansile growth of the pituitary neoplasm, the effect of the elaboration of excessive quantities of pituitary hormones, and the interference with other normal pituitary functions by pressure of the tumor upon the uninvolved portion of the gland.

Local Effect of Increase in Size of the Anterior Lobe of the Pituitary: If the pituitary gland enlarges to a great extent, it produces pressure on the surrounding sella turcica and diaphragma sellae. This results in erosion of the bony wall, increase in size of the sella, and a bulging of the diaphragma (Fig. 1). The tumor may extend through the floor of the sella into the sphenoid sinus and project upward through the diaphragma sellae (3).

The Effects of Abnormal Quantities of Pituitary Hormones: The pituitary tumor produces an excessive amount of growth hormone or somatropin, which is responsible for the most obvious manifestations of the disease. All of the tissues of the body are affected but show a peculiar variability in the extent of involvement, apparently determined in part by the genetic make-up of the individual and the response of the tissues to the stimulus of the circulating hormones. Another factor may be the extent of imbalance of the various hormones of the body (2, 22).

The folds of the skin and scalp become accentuated. The thickening of the skin is due primarily to increased connective tissue, but other elements, including the epithelium and the hair follicles, are also increased in size. There appears to be an unusual type of edema producing additional swelling (Fig. 4, B). Connective-tissue hyperplasia has been described in the supporting network of the bronchi, the periportal connective tissue of the liver, and the interstitial tissue of the pancreas (9), heart (16), and other organs. It is apparent in the supporting structures of the skeleton: the ligaments, tendons, fascia, articular capsules, and stroma of the synovial linings of joints.

Cartilage is also increased extensively in acromegaly. The stimulus to proliferation appears to involve all cartilage, irrespective of its function.

Patients with acromegaly frequently complain of pain in the joints and extremities. In 16 of 25 patients studied by Kellgren (18) pain was a prominent symptom. In 3, painful swelling of the finger joints, considered to be rheumatoid arthritis, was the presenting symptom. The joints are enlarged by a combination of thickening of the synovia, bursae, cartilage, ligaments, capsule, and bone, accompanied by intra-articular effusion (Fig. 4, B).

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The most spectacular alterations induced by large amounts of growth hormone secretion are those occurring in the skeletal system. If the bones are affected before the epiphyses unite with the metaphyses, endochondral ossification is accelerated. This results in an increased length of the tubular bones and the clinical syndrome of gigantism. In most cases acromegaly has its onset during puberty or later, so that there is little, if any, increase in height. In this discussion we are concerned with the manifestation of the disease developing shortly before or after the epiphyses are closed.

Although growth is not possible at epiphyseal cartilages which have become obliterated, endochondral growth does occur at special sites. Cartilaginous proliferation and subsequent ossification take place at the mandibular condyle and produce an elongation of the mandible. Weinmann and Sicher (26) and Waine, Bennett, and Bauer (25) state that some endochondral bone formation occurs in the deep layers of the articular cartilages. This will increase the length of the tubular bones after obliteration of the epiphyseal cartilage to some extent, but this must be very limited.

A considerable degree of cartilage proliferation and endochondral ossification takes place at the costochondral junctions (18, 25). At the same time the perichondrium covering the outer margins of the costal cartilage is transformed into a sheath of periosteum which produces bone continuous with the osseous shaft of the rib. As a result of the excessive cartilage proliferation and endochondral and appositional bone formation, the ribs and costal cartilage become longer and are broader at their sternal attachments. The increasing length of the ribs results in a larger chest cavity (Fig. 3) and probably contributes to the kyphosis of the thoracic spine.

Under the influence of the excess secretion of growth hormone in adults, bone growth as a result of periosteal apposition is more extensive than endochondral ossification. Appositional growth of bone is found primarily in those bones or parts of bones where growth normally occurs throughout life. The spurs present about the joints in elderly persons can be considered to be part of the normal growth or aging process, although they may be increased when the bone is subjected to unusual stress (4). Absence of spurs from the vertebral margins in later life may be an indication of osteoporosis, in which there is deficiency in bone production throughout the skeleton.

In acromegaly, periosteal appositional bone growth is accelerated, resulting in an early appearance and increased size of the tuberosities at sites of muscular and ligamentous attachments. There is a general increase in thickness of the bones, easily identified in some cases in the calvarium, vertebrae, phalanges, facial bones, ribs, and long bones.

As a result of the overgrowth and elongation of the mandible, the lower teeth overlap the upper. The upper teeth then come in contact with the inner lingual surface of the lower, thus producing a mechanical force which causes a migration of the teeth outward and an increase of the space between them. This wedge-like action of the upper dental arch may be intensified by the pressure of the hypertrophied tongue (26). Hypercementosis and extensive resorption of the roots of the teeth are stimulated by the enhanced traction on the forcibly separated teeth.

It is not generally known that the accelerated growth of acromegaly is accompanied by excessive bone resorption in some regions of the skeleton. Many authors (1) have described generalized osteoporosis as a prominent feature of this disease although it has been absent in most of our cases. An example of localized resorption of bone is seen in the enlargement of the paranasal sinuses. This is a dual process, initiated by the surface apposition of bone which increases the size of the sinus cavity. In the frontal sinus region, it may produce a bulging of the superciliary ridges which is most promi-

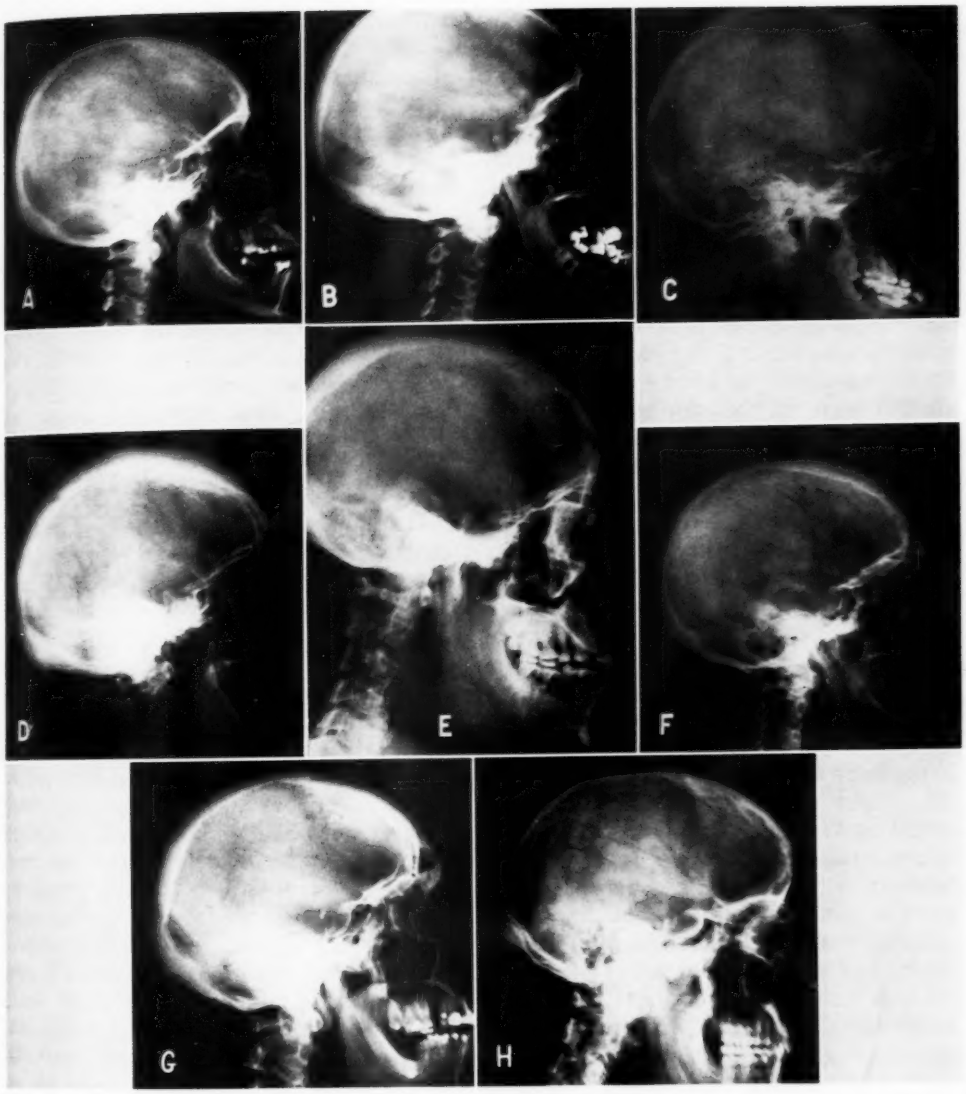

Fig. 1. Representative examples of skulls arranged in order of increasing size of sella turcica. The shape and size of the sella vary considerably. The shape in C, in which the sella is deepest posteriorly, was the most common, being seen in 12 of 27 patients. The oval shape of H was present in 10 patients. Five patients had rounded sellas. A and B are considered to be normal. The variations in size and shape of the mandible are illustrated by E and F. There is a sex difference in the appearance of the skulls; B, E, G, and H are males. They have more prominent supraorbital ridges than the females, independent of the size of the frontal sinuses.

nent in males (Fig. 1). The mastoid processes also increase in size by external deposition of bone and the air cells by internal resorption. The sinuses of the normal adult person enlarge throughout life but at such a slow rate that the increase usually cannot be detected on roentgenograms obtained over a period of ten years.

All normal tubular bones are constantly undergoing periods of bone apposition, alternating with bone resorption. In growing children and in most of the tubular bones of acromegalic patients, the ap-

positional growth is greater than the resorptive process, so that the end-result is an increase in bone mass. In acromegaly resorption of the outer surface of the shaft may predominate in some of the tubular bones and produce a very narrow bone with a sudden flaring at the ends. The cortex is of normal or increased thickness so that there is encroachment upon the marrow cavity. This condition was described by Curschmann (8) in 1906 and von Bonin (6) in 1912, and was more recently emphasized by Kellgren (18). This excessive modeling resorption is usually seen in the proximal phalanges and the metatarsals of the feet, but may also be present in the metacarpals and other tubular bones (Fig. 6). Occasionally it may be noted in the metatarsals of normal elderly individuals but not nearly so frequently as in acromegalic patients.

The mandible deserves special consideration, since it may exhibit the processes of endochondral ossification, periosteal apposition, and modeling resorption occurring simultaneously along different surfaces. The endochondral ossification which forms bone at the articular surface of the condyle has already been described. This separates the mandible from the maxilla, allows space to accommodate the apposition of bone along the alveolar ridge and the continued eruption of the teeth, and also produces prognathism. The chin becomes prominent as a result of apposition of bone along the mental tuberosity. Appositional bone is formed at other surfaces, also, such as the tip and posterior border of the coronoid process and the posterior border of the ramus.

Molding resorption acts especially on the anterior margin of the condyloid and coronoid processes along the entire anterior border of the ramus and the angle. As a result of the resorption, the angle is inclined steeply upward and presents more marked concavity than normal. The end-result of the changing contour of the mandible in some cases is to increase the size of the mandibular angle between the ramus and the body (Fig. 1, B and F). This can be measured by drawing lines tangential to the prominent outer surfaces of the mandible on the lateral roentgenogram and measuring the angle subtended by them. The final appearance of the mandible of acromegalic patients varies considerably, depending upon the degree of preponderance of the processes of bone production and bone resorption.

There is a remarkable splanchnomegaly in these patients which appears to exceed even the enlargement of the skeletal parts (9, 16). This is partly the result of the connective-tissue proliferation but is due also to hyperplasia and hypertrophy of the differentiating functional cells of the organ. Cushing and Davidoff described an enlargement of the lungs, heart, liver, kidneys, spleen, bowel, endocrine glands, and other visceral organs, but noted an exception in the brain, which generally is of normal weight. Associated with the visceromegaly there is frequently, but not necessarily, an augmentation of function.

ROENTGENOLOGY

There have been few articles devoted to the roentgen evaluation of patients with acromegaly. The only recent published report in the radiological literature was one by Moore (20), who was primarily concerned with a syndrome of acromegaly, toxic goiter, diabetes mellitus, and hyperostosis of the vault of the skull. Moore also described some of the cranial manifestations of the disease in his book, *Hyperostosis Cranii* (21). An excellent description of the clinical findings and some of the roentgen signs associated with involvement of the limbs and joints is given by Kellgren, Ball, and Tutton (18). Finlay and MacDonald (14) published a thorough evaluation of the roentgen findings in 12 cases.

Members of the endocrine division of the University of California Medical Center have been interested in this disease for many years. When a recent study of the clinical aspects was undertaken, it was thought that an evaluation of the

TABLE I: DEGREE OF INVOLVEMENT OF DIFFERENT ORGANS OR REGIONS OF THE BODY IN ACROMEGALY

	Female		Male	
	Present	Absent	Present	Absent
HEAD				
Calvarium				
Hyperostosis	14	2	5	6
Increased thickness	10	6	3	8
Sella turcica enlargement	13	3	9	2
Sinus enlargement				
Frontal	4	12	6	5
Maxillary	2	14	4	7
Mastoid enlargement	1	15	2	9
External occipital protuberance enlargement	9	7	11	0
Mandible				
Elongation	2	12	1	5
Widening			2	
CERVICAL SPINE				
Increased height	0	12	0	7
Increased length	2	10	0	7
Hypertrophic spurs	7	5	6	1
Thick intervertebral disk	1	11	2	5
THORACIC SPINE				
Increased height	0	16	0	10
Increased length	1	15	4	6
Increased width	0	16	0	10
Hypertrophic spurs	14	2	7	3
Thick intervertebral disk	0	16	0	10
LUMBAR SPINE				
Increased height	0	16	0	7
Increased length	0	16	0	7
Increased width	0	16	0	7
Hypertrophic spurs	12	4	7	0
Thick intervertebral disk	4	12	4	3
HANDS				
Thick soft tissues	14	1	11	0
Large tufts of distal phalanges	12	3	11	0
"Squared" bases of distal phalanges	14	1	9	2
Exostoses of phalanges, metacarpals, or carpals	14	1	9	2
Thick shafts of tubular bones	4	11	9	2
"Squared" radius or ulna	7	8	6	5
Thick articular cartilage	8	7	5	6
FEET				
Thick soft tissues	10	4	8	1
Large tufts of distal phalanges	14	0	7	2
"Squared" bases of distal phalanges	14	0	9	0
Exostoses of phalanges, metacarpals, or carpals	13	1	7	2
Thick shafts of tubular bones	2	1*	2	2†
Thick articular cartilage	8	6	5	4

*9 were decreased in thickness.
†5 were decreased in thickness.

roentgen manifestations would be profitable. Of those patients undergoing extensive laboratory procedures, 27 were chosen because of their availability for roentgen surveys. These cases were unselected and represent a random sampling of the group. There were 16 females with an average age of forty-seven years and a range of thirty to seventy-three years. The average age of the 11 males was forty-three years, with a range of twenty-four to fifty-three years.

In reviewing the roentgenograms it soon became apparent that very few showed the advanced changes commonly associated with acromegaly. This may be attributed to the acumen of the clinicians responsible for detecting and treating the disease. There was also very little correlation between the degree of involvement of different organs or regions of the body (Table I).

Calvarium (Fig. 1): There are certain differences in the male and female skull which one would expect to see exaggerated with an excessive growth stimulus. Hyper-

ostosis of the inner table of the frontal bone of the skull and diffuse hyperostosis of the calvarium are seen much more commonly in females. The incidence of hyperostosis of the inner table is increased in acromegaly, and was present to some degree in 19 patients of the 27 for whom adequate roentgenograms were available. In 10 cases this change was moderately to far advanced, in 9 of the 16 females and only 1 of the 11 males. The same was true of the thickness of the calvarium. This was estimated at the point of maximum thickness along the convexity of the cranium and did not include areas of hyperostosis or the external occipital protuberance. The calvarium was thought to be significantly thicker than average in 10 of the 16 females and in 3 of 11 males. This is contrary to the experience of Moore, who believes that calvarial thickening is seen only exceptionally, if at all, in acromegaly. It is accepted, however, by most investigators as a feature of the disease and was thought to be present in 6 of the 12 cases of Finlay and MacDonald. Hyperostosis and skull thickening in the present series were not necessarily concomitant features, as 2 female skulls without hyperostosis were significantly thickened and 3 females without thickening had hyperostosis.

Measurements of the thickness of the calvarium were made at the widest part of the frontal or parietal bones on the lateral roentgenograms. The average thickness for females was 1.6 cm. and for males 1.42 cm., with ranges of 0.8 to 2.3 cm., and 0.8 to 2.0 cm., respectively.

Inasmuch as a thick, undulating scalp is sometimes detected clinically, it was also measured, at its thickest part, on the lateral roentgenogram. The average measurement for males was 1.29 cm. compared to 0.89 cm. for females.

Sella Turcica: No attempt was made to measure the size of the sella turcica, as it was felt that the estimation of an experienced radiologist was superior to any available methods of quantitative evaluation. In 15 skulls, the fossa was moderately or greatly enlarged, and in 6 others minimal enlargement was thought to be present. A normal-sized fossa was present in 5 (19 per cent) of the 27 roentgenograms examined, but in 2 of these cases there was evidence of erosion of the floor of the sella, leaving 3 of the 27 patients with no roentgen evidence of a pituitary tumor. The distance between the anterior and posterior clinoid processes was increased in 9 of the 27 skulls, indicating that the tumor had extended above the diaphragma sellae. The shape of the enlarged sella varied considerably. One sixty-nine-year-old patient had a moderately enlarged sella within which there was extensive calcification. In some patients the anterior and posterior clinoid processes were thickened by appositional bone growth. There was no difference in incidence of sellar changes between the sexes (Fig. 1).

Sinuses: The frontal sinuses were enlarged in most of the males (6 of 11 patients) but in only one-fourth of the females (4 of 16 patients). This is in agreement with the greater prominence of the supraorbital ridges and the larger frontal sinuses normally seen in males. The size of the maxillary sinuses is more difficult to evaluate but the estimated size compared well with the frontal sinuses. Two of the 16 females and 4 of the 11 males were thought to demonstrate some degree of enlargement.

Mastoids: Normal mastoids vary so widely in size and degree of pneumatization that it was found difficult to evaluate possible changes. However, in 3 patients there appeared to be definite mastoid enlargement.

External Occipital Protuberance: The external occipital protuberance varies in size. It is sometimes very large in normal persons, with a tendency to increase in size with age. It was assessed as large in 9 of the 16 females and in all of the 11 males.

Mandible: The length of the mandible could not be estimated on all of the lateral roentgenograms of the skull because the distal end was frequently not included.

Since the longer mandibles were most likely to reach beyond the margin of the film, the estimations of length are probably too low. The mandible was regarded as elongated if its occlusal surface extended significantly beyond that of the maxilla or if the mental tuberosity were unduly prominent. Of those mandibles that were projected on the roentgenogram in their entirety, 2 of the 14 in females were elongated, and only 1 of the 6 in males. Two of the males with mandibles of normal length showed marked widening of the mandibular body (Fig. 1).

Although one of the classical findings of acromegaly is a widening of the mandibular angle, this was not found to be a constant feature in the present group of cases. The average condylar angle, as measured by the intersection of lines drawn tangential to the outer surfaces of the body and ramus, was 127° in females and 117° in males. There was a wide range: from 120 to 144° in females, and from 100 to 138° in males.

Dental surveys were not conducted in all patients, but the absence of all, or almost all, of the teeth was noted in 6 of the 16 females and in 4 of the 11 males. The presence of hypercementosis and spreading of the teeth was observed in some, but not in all patients.

Spine: Elongation and widening of the vertebral bodies due to the periosteal apposition of bone along the anterior and lateral surfaces were well demonstrated in Erdheim's (11) classic case, and have been described as a characteristic feature of acromegaly by others (14, 27). Epstein (10) reviewed the spines of his last 18 cases of the disease without finding evidence of vertebral change.

Roentgenograms of the cervical spine in 19 patients, thoracic spine in 26 patients, and lumbar spine in 23 patients were reviewed for evidence of elongation, widening, increased height, growth of the zygapophysial joints, hypertrophic spurs, and abnormalities of the intervertebral disks. Some lengthening of the vertebral bodies was seen in 2 of the cervical spines and in 5 of the thoracic spines, but similar changes have been seen in normal middle-aged and elderly individuals and were not regarded as characteristic of the disease. Hypertrophic spurs of the margins of the vertebral bodies were present in several patients, but the extent of involvement was not greater than in the general population. As would be expected, this was greater in males than in females. Some enlargement of the articular facets was noted in 3 cervical and 2 lumbar spines. The most impressive finding in the spine was an increased thickness of the lumbar intervertebral disks in 8 patients, and of the cervical disks in 3. Several of these thickened disks were located between vertebrae with hypertrophic spurs, which is contrary to the usual association of narrowed disks with hypertrophic vertebral changes (Fig. 2, B). In the thoracic region the intervertebral disks were not thick and in 11 of the 26 cases studied were narrowed. These narrowed disks appeared to be associated with

Fig. 2. Lateral roentgenograms of the thoracic (A) and lumbar (B) spine of a patient having a marked concavity of the central posterior portions of the vertebral bodies. The intervertebral disks in the thoracic region are usually narrow in contrast to the wide disks in the lumbar region.

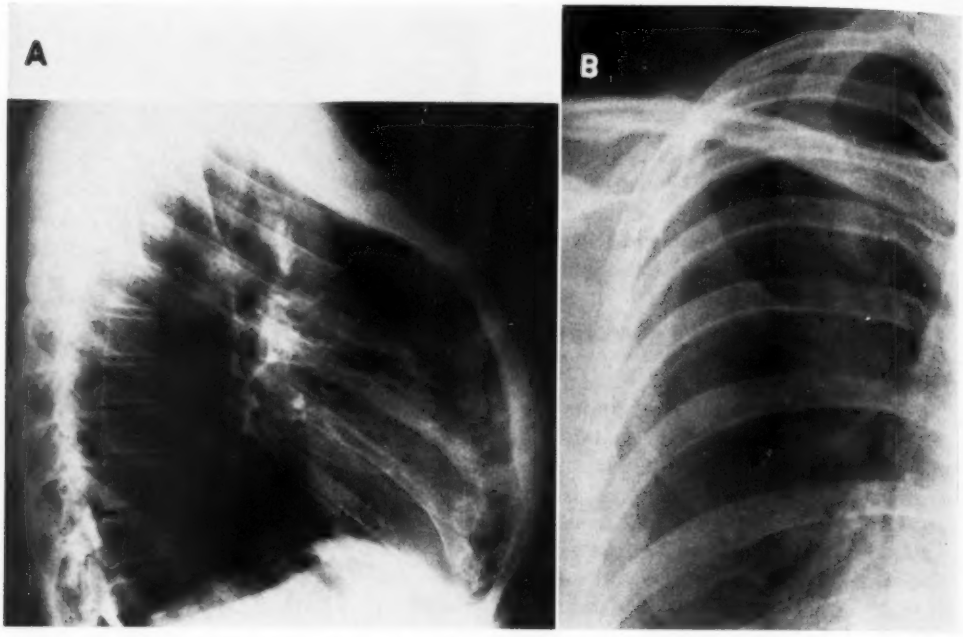

Fig. 3. A. Increased anteroposterior diameter of the chest due to the elongation of the ribs and costal cartilages. The sternum is displaced forward. The manubrium assumes a more horizontal position than usual. This patient does not have a kyphosis.
B. Accentuation in size and irregularity of the flared lower border of the posterior portion of the ribs.

a thoracic kyphosis which was a frequent finding in these patients.

An unusual appearance of the posterior aspects of the lumbar or thoracic vertebral bodies was seen in 6 patients, consisting of a marked exaggeration of the normal posterior concavity (Fig. 2, A and B). Similarly shaped vertebrae are seen in patients with spinal cord tumors.

Ribs: In most cases the thorax was enlarged as a result of elongation of the ribs. This enlargement was manifest roentgenologically by increased sagittal and coronal thoracic diameters (Fig. 3, A). The lower portion of the sternum was in some cases elevated and an increased angulation at the sternal angle was evident as the manubrium assumed a more horizontal position, a result of lengthening of the lower and middle ribs to a greater extent than of the upper ribs.

Finlay and MacDonald found a fusiform widening at the costochondral junctions on the roentgenogram in 50 per cent of their cases. At autopsy, Waine, Bennett, and Bauer observed a considerable enlargement in all directions at the costochondral junctions and an investment of the cartilage by a sheath of bone continuous with the osseous shaft. An attempt was made to confirm these findings. The size of the distal ends of the ribs varies so greatly, however, and enclosure of the chondral cartilage by bone occurs so frequently in normal persons that no quantitative studies were done. The general impression was that in some patients the costochondral junction was excessively wide.

In several patients there was a thickening of the ribs, particularly the flared lower border, which had an undulating, wavy surface (Fig. 3, B).

Hands and Feet: Adequate examinations of the hands of 26 patients and the feet of 23 patients were obtained. The most frequent abnormality was a marked thickening of the soft tissues of the fingers

and toes. This was recognized in all of the hands except for those of 1 female, and in all of the feet except in 4 females and 1 male. The thickening was particularly prominent about the proximal interphalangeal joints of the fingers because of the involvement of the joint capsule and synovial lining, producing a fusiform shape similar to that seen in rheumatoid arthritis (Fig. 4, B). Three of the 25 patients of Kellgren *et al.* had presenting changes in the finger joints initially considered to be rheumatoid arthritis. Enlargement of the limb joints was noted in all of their patients. The fat of the subcutaneous tissue and that surrounding the muscle was replaced in some cases by fibrous tissue resulting in a characteristic homogeneous appearance of the soft tissue. The normal fat shadows were thus obliterated, so that the skin, muscles, and articular capsules could not be identified.

The tufts of the terminal phalanges of the hands were large in 23 of 26 patients, generally greater in males than in females. A similar enlargement of the terminal tufts of the distal phalanges of the toes was present in 21 of 23 patients. The bony proliferation of the tufts involves the distal, lateral, and anterior surfaces and tends to overhang or envelop the shafts.

The bases of the distal phalanges were also frequently enlarged, with broadening out of proportion to that of the shaft, and elongation distal to the joint. Exostoses arising from the base and extending distally were present in some cases. These were frequently very large, particularly when arising from the base of the great toes. Similar changes are seen in normal feet but are usually less extensive.

In 23 of the hands and 20 of the feet bony projections or small exostoses were present in the periarticular surfaces at the ends of the bones and along the shafts in the regions of tendon or ligamentous insertions. This change was best seen in the heads of the metacarpal bones.

Thickening of the shafts of the phalanges, metacarpals, and metatarsals has been described as a characteristic feature of acromegaly but in our series was present in only one-half of the hands and 4 of the feet. The thickening of the tubular bones of the hand was greater and more frequent in males (9 of 11 cases) than in females (4 of 16 cases). When present, it involved both the cortex and the medullary cavity (Fig. 5).

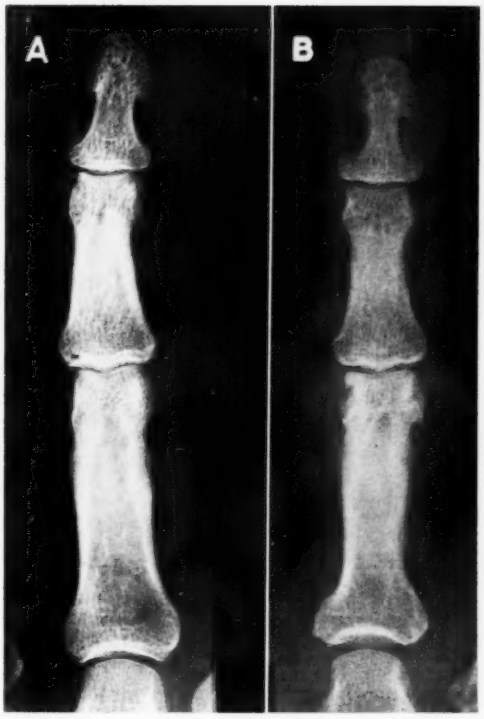

Fig. 4. A. The patient was a normal husky middle-aged laborer. The soft tissues are thick, but not nearly as thick as in most patients with acromegaly. The ungual tufts of the distal phalanges are as large as in several of the patients with acromegaly.

B. Finger of an acromegalic patient with minimal bony changes. The outstanding feature was a marked thickening of the soft tissues of the fingers, most prominent about the proximal interphalangeal joint, producing a fusiform shape. The subcutaneous fat line is partially obliterated but is visible in the proximal part of the finger, demonstrating the increased thickness of the dermis. This thickening of the soft tissues in the hands is the most constant feature of acromegaly.

Paradoxically, the shafts of the proximal phalanges of the feet were usually narrowed. The constriction involved the entire circumference of the shaft and was generally at the expense of the medullary cavity. The appearance was that of

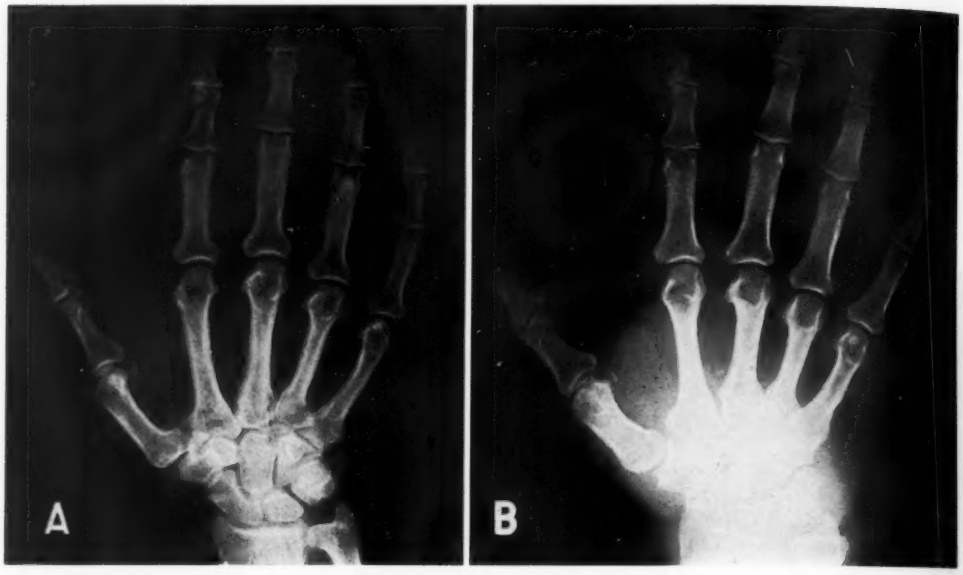

Fig. 5. Demonstration of the variation in the appearance of the hands.
A. Moderate bony exostoses, which are greatest at the heads of the metacarpals. The metacarpophalangeal joint spaces (articular cartilage and synovia) are thickened despite the hypertrophic changes of the adjacent bone.
B. In this patient the hypertrophy of the ungual tufts and bases of the distal phalanges is out of proportion to the hypertrophic changes of other bones.

narrow pipes of constant caliber, ballooning out abruptly at the head and base. The ends were squared and exhibited the bony prominences and small exostoses characteristic of the disease. This is a result of excessive molding resorption at the periosteal surface. Constriction of the shafts of the proximal phalanges was present in 14 of the patients and involved both sexes. In 4 cases a similar deformity of the metatarsals was also present. One patient had roentgenograms of the feet taken at intervals of ten years. On the initial examination the proximal phalanges were of normal caliber; on the later films the shafts were much narrower (Fig. 6).

Increased thickness of the articular cartilages of the joints of the hands and feet was inferred in over one-half the cases, from the wide separation of the adjacent bony articular surfaces. The distance between the bones was as much as twice the normal. Some degree of cartilage proliferation appeared to be present in 13 hands and 13 feet. The thickened cartilages were frequently associated with large bony tuberosities and exostoses of the periarticular surfaces of the bones. This finding serves to differentiate the hypertrophic changes from those of osteoarthritis, in which the cartilages are normal or narrowed.

Changes similar to those described in the tubular bones of the hands and feet were seen also, but to a lesser degree, in the long bones of the extremities. These consisted of periosteal bone formation, most pronounced at the ends of the bones, which produced a sharp transition between the shafts and the wider proximal and distal portions. Exaggerated bony tuberosities, hypertrophic changes, and thickened articular cartilages were seen in some cases. These were most obvious at the distal end of the radius and ulna and at the distal end of the femur and proximal end of the tibia. Since roentgenograms were not obtained of all the long bones, no statistical analysis will be attempted.

Sesamoid bones participated in the general bony overgrowth and were frequently quite large with irregular surfaces.

Osteoporosis has been described as a frequent occurrence in patients with acromegaly. The disease has been said to resemble the postmenopausal state in that both show (*a*) a high serum inorganic phosphorus level, (*b*) negative calcium and phosphorus balance and a tendency to osteoporosis, and (*c*) a drop in serum phosphorus and retention of calcium and phosphorus with estrogen therapy. Osteoporosis was not a conspicuous feature in our group of cases. It was present to a significant degree in only 3 females of fifty-one, sixty-nine, and seventy-three years.

Fig. 6. Dorsoplantar roentgenogram of the foot. The shafts of the proximal phalanges and the distal portion of the shafts of the metatarsals are markedly narrowed. There is an abrupt transition between the narrowed shafts and the enlarged ends of the bone. The narrowing is at the expense of the medullary cavity and involves the regions of bone in which there is a thick cortex of compact bone. It spares the spongy bone of the metaphyses and epiphyses.

Viscera: The heart and aorta were judged to be large in 11 of 18 patients who had adequate roentgenographic studies.

Fig. 7. Intravenous urogram. The kidneys are enlarged, the increased size involving both the parenchyma and calyces.

The kidneys were assessed on plain roentgenograms of the abdomen, and in some cases intravenous urographic studies were performed. The kidneys appeared large in 8 of 17 cases. Where urograms were obtained, both the renal parenchyma and the calyces and pelvis were found to be increased in size (Fig. 7).

Barium enema studies were done in 4 cases. In all, the lumen of the colon was judged to be minimally or moderately increased in caliber and length.

In 1 case an extraperitoneal pneumogram revealed what appeared to be normal-sized adrenals.

Effects of Therapy: One of the aims of undertaking this investigation was to find a method of determining whether the disease was active or quiescent, and, if active, whether subsequent therapeutic measures were successful.

Several patients were observed over

periods of many years, but evidence of continued growth of the bones was seen in only a few. In 19 cases cephalometric measurements were made on repeated lateral skull films without demonstrating significant measurable changes in the calvarium, sinuses, or facial bones in any instance. Sixteen of the 19 patients, however, showed no clinical signs of activity over the years of study. Undoubtedly, bone growth will be observed in active untreated cases if the disease is followed over a sufficiently long period, but this would be of little value in determining the degree of activity at any specified time. Once the bone has increased its size, it does not diminish even though the quantity of circulating growth hormone is decreased by adequate surgical or radiation therapy.

Cushing and Davidoff observed a surprising diminution not only in the apparent but in the measured size of the hands and feet within a day or two after operative removal of the pituitary tumor. Some physicians have used the quantity of water displaced by immersing the hands as a means of estimating changes in volume of tissue (17). The difficulty of reproducing the exact technic of measurement has made this method impractical.

It was hoped that the decrease in thickness of the soft tissues due to treatment could be determined roentgenographically. Measurements were made of the thickness of the scalp on lateral roentgenograms of the skull, and of the soft tissue adjacent to the phalanges on posteroanterior views of the hands. A definite reduction in the thickness of the scalp was observed in 1 patient subsequent to roentgen therapy of the pituitary. In 2 other patients a very slight decrease in the thickness of the soft tissues of the phalanges was seen. These changes, however, were much less than anticipated and in many instances were not measurable, although the patients noted a remarkable subjective improvement in the thickness of the skin and decreased ring and shoe size. In no case did the soft tissues revert to normal size, and any change that occurred represented a very small part of the total amount of soft tissue. Because of the rapidity of the response and its limited degree, it must be concluded that the decrease in soft tissues is related to changes in their fluid content, and that the thickening due to connective-tissue hyperplasia persists.

A reduction in size of the sella turcica and thickening of the cortex in areas of erosion occurred in several patients following roentgen therapy. In some cases the sella decreased considerably in size but did not show a complete return to normal, although the disease appeared clinically to be quiescent.

Pneumoencephalography, with small quantities of gas to demonstrate the suprasellar cisterns in those patients in whom the tumor extends above the sella, is an excellent method of following the response of the tumor to irradiation. This technic is of no value where the tumor erodes the floor of the sella and does not extend above the diaphragma sellae.

DISCUSSION

The diagnosis of acromegaly is primarily clinical. The roentgen diagnosis could be accurately established in an examination of the skull if the sella turcica were significantly enlarged and if this finding were accompanied by an elongated mandible with a wide angle and enlarged sinuses. The presence of a thick scalp and of hyperostosis of the inner table of the skull in women would further substantiate the diagnosis. This combination of morphological changes, however, was present in only a few of our patients, and in many cases a diagnosis of the disease by roentgenographic methods alone was not feasible. All of these findings, with the exception of enlargement or erosion of the sella turcica, can be found in some apparently normal individuals. This is true also of other accepted diagnostic roentgen criteria such as enlargement of the tufts of the terminal phalanges, widening of the tubular bones, hypertrophic spurring at tendi-

nous insertions, and enlargement of the vertebral bodies.

Of particular significance in this study was the presence of a marked thickening of the soft tissues, best seen in the fingers and toes. Without this finding the diagnosis of acromegaly should be looked upon with suspicion. This thickening is slightly less if the disease is quiescent, but is still quite obvious. The presence of thick soft tissues is not diagnostic of acromegaly but their absence is highly significant.

Another pertinent observation is the association of thickened articular cartilages (wide joint spaces) of the hands and wrists with hypertrophic changes of the adjacent periarticular surfaces. Similar periarticular spurs are seen in osteoarthritis but in those cases the cartilages are not thickened. Ultimately, the acromegalic joint may be involved in a degenerative process, in which case it cannot be differentiated from osteoarthritis.

A peculiar constriction of the shafts of the proximal phalanges and metatarsal bones of the foot was observed in most of the patients. This has been seen in a few normal subjects but must be quite rare. The results of this study indicate that roentgenograms of the feet should be obtained along with those of the skull and hands in the routine evaluation of acromegaly.

The concave posterior borders of the lumbar vertebrae observed in 6 patients have not been commented upon in previous publications on this subject. They are to be seen, however, in Figure 1 of an article by Chester and Chester (7), and also in Figure 1583 of Schinz's textbook *Roentgen Diagnostics* (23). This change could be due to increased molding resorption of the central posterior surfaces of the vertebral bodies as a direct result of the excessive quantity of growth hormone or, secondarily, of pressure by the enlarged soft tissues in the spinal canal. The appearance resembles that of the lobulated posterior surfaces of the spinal column sometimes seen in patients with soft-tissue tumors of the spinal canal.

SUMMARY

(1) Acromegaly is the result of increased secretion of growth hormone by a benign or, rarely, a malignant tumor of the anterior pituitary occurring during or after closure of the epiphyseal cartilages.

(2) Symptoms and signs are due to (*a*) the expansile growth of the neoplasm, (*b*) the elaboration of excessive quantities of pituitary hormone, and (*c*) the interference with other normal pituitary functions by pressure of the tumor upon the uninvolved portion of the gland.

(3) All the tissues in the body are affected by the excessive quantity of growth hormone. In general, the response is one of hyperplasia and hypertrophy. The bones may increase in size due to accelerated endochondral ossification or appositional bone growth. In some areas there is increased bone resorption.

(4) Some of the changes occurring in the bone are similar to those incident to the normal aging process, but are markedly accelerated and greater in degree.

(5) The usual sex differences in the appearance of the soft tissues and skeleton are exaggerated by the excessive quantity of growth hormone.

(6) Roentgenologically, the most constant feature is an increase in thickness of the soft tissues of the fingers, toes, and scalp. This diminishes after successful treatment by irradiation or surgical removal of the pituitary gland, but the tissues do not revert to normal size.

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SUMMARIO IN INTERLINGUA

Acromegalia

Certes del alterationes que occurre in le ossos in casos de acromegalia es simile al alterationes incontrate in association con le processo normal de invetulation. Tamen, illos es marcatemente accelerate e plus alte in grado. Le usual differentias sexual in le apparentia de histos molle e del skeleto es exaggerate per le quantitate excessive de hormon de crescentia.

In un recente studio del aspectos clinic de acromegalia al Centro Medical del Universitate California, 27 patientes adulte —16 femininas e 11 masculos— esseva seligite pro un evalutation roentgenologic. Viste que omne le histos del corpore es afficite, studios detaliate del cranio, del columna vertebral, del thorace, del histos molle, del extremitates, e del visceres esseva effectuate. Roentgeno-diagnoses pote esser establite accuratemente in un examine del cranio si le sella turcic es allargate significativemente e si iste constatation es accompaniate del presentia de un mandibula elongate a angulo aperte e sinos allargate. In feminas, le constatation de un spisse epicranio e de hyperostosis del tabula interior del cranio corrobora, il pare, le diagnose additionalmente. Tamen, iste combination de alterationes esseva presente in pauc patientes solmente, e in multe casos un diagnose exclusivemente roentgenologic non esseva practicabile. Omne le constatationes con le exception de allargamento o erosion del sella pote esser trovate in individuos qui es apparentemente normal. Le plus constante characteristica esseva un augmentate spissitate del histos molle in le digitos manual e pedal e in le tegumento cranial. Spisse cartilagines articular (i.e. large spatios articular) in le manos e carpos esseva associate in certe casos con alterationes hypertrophic

del adjacente superficies periarticular. Simile sporones periarticular es trovate in casos de osteoarthritis, sed alora le cartilagines non es spissificate. Concave margines posterior del vertebras lumbar, observate in 6 patientes, ha previemente non essite commentate.

Le alterationes post-therapeutic esseva multo inferior al expectationes. In multe casos illos non esseva mesurabile, sed le patientes notava un remarcabile melioration subjective in le spissitate de pelle e in le calibre de anellos e del calceatura. Nulle del casos monstrava un reversion a dimensiones normal in le ossos e le histos molle. Il es necessari concluder que le spissification resultante de hyperplasia del histos conjunctive es un phenomeno persistente. In certe casos le dimensiones del sella decresceva considerabilemente post le tractamento, sed illos non retornava al stato normal.

Familial Pulmonary Alveolar Microlithiasis: Four Cases from Colombia, S. A.

Is Microlithiasis Also an Environmental Disease?[1]

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PULMONARY alveolar microlithiasis is characterized by the presence of innumerable minute concrements lying free within the alveoli, throughout the lungs, unattached to the alveolar walls. The disease is extremely rare; not more than 50 cases have been reported in the literature. Since symptoms are usually absent, the diagnosis is almost always made during a routine examination of the chest, when the roentgenologist is surprised to discover the disease in an advanced stage in an apparently healthy person. These two features, namely, a characteristic roentgenogram showing the presence of innumerable minute intra-alveolar concrements, like grains of sand, and the complete absence of symptoms, make possible a radiologic diagnosis even without a confirmatory pathologic report.

The first case of microlithiasis was reported by Harbitz (1) in 1918, and the second by Schildknecht (2) in 1932. Schildknecht described for the first time the roentgen features, but Puhr (3) gave the disease the name of pulmonary alveolar microlithiasis, by which it is now known. Five more cases were reported between 1947 and 1953 (4–8). The remainder were published subsequently (9–11, 15–21).

An interesting feature of the disease, as reported in the literature, is that it has on several occasions been observed in members of a single family (9, 10, 11). The 4 cases of pulmonary alveolar microlithiasis to be reported in this article, occurring in 4 sisters, are the first to be discovered in Colombia. So far as can be determined from a thorough review of the literature at our disposal, they are the only cases of the disease ever reported from South America. One of the patients died, and the clinical diagnosis of pulmonary alveolar microlithiasis was confirmed at autopsy.

In patients with pulmonary alveolar microlithiasis, death occurs as a result of cardiac insufficiency, which in its turn is due to chronic cor pulmonale developing after ten, twenty, or more years of apparently good health. The early symptoms are those of discrete pulmonary insufficiency, which manifests itself over a more or less prolonged period by dyspnea and cyanosis on extreme exertion.

In regard to etiology, it can be stated that the disease is none of the following conditions: an infection, an inflammatory process, a tumoral lesion, a pneumonoconiosis, or the result of either an endocrine or a circulatory disorder. It is generally believed that, through the influence of certain unknown factors, there is a disturbance in the respiratory metabolism of carbon dioxide, which promotes alkalinity at the alveolar surface, with consequent precipitation of the microliths.

The familial nature of the disease has been explained on the basis of hereditary congenital predisposition. We believe, however, that the causal role of environment, dietetic factors, and living conditions cannot be overlooked. The four sisters who are the subjects of this report have always lived in the same house and locality,

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on the same diet, and under the same living conditions.

In the first patient, the disease was discovered in June 1948, during a roentgen examination of the chest, by Dr. Marino Barona (22), who consulted with us because of the unusual findings, unlike those of any pulmonary lesions known up to that time. A second roentgenogram, taken with greater penetration and with the Bucky, was of no help in clarifying the diagnosis. The films were therefore sent to Dr. M. C. Sosman of Boston, who replied that he had had an opportunity, a few years before, of observing two patients with similar chest roentgenograms. He designated the disease as pulmonary calcinosis but had been unable to find any description of this condition in the literature. Several years later, Dr. Sosman informed us that one of his patients had died and the autopsy findings enabled him to classify the disease as pulmonary alveolar microlithiasis. Dr. Sosman also informed us that the chest roentgenograms of a brother of his patient showed lesions of the same kind and asked that we try to obtain films of the family in our case. With some difficulty the first patient and one of her sisters were persuaded to make the journey to Bucaramanga in April 1956, and chest films were taken. In the original patient, the disease had progressed markedly, but she was still asymptomatic. To our surprise, the chest roentgenograms of the sister showed her to be suffering from the same condition, though her pulmonary lesions were less advanced than those observed in the first patient eight years earlier. These two cases are presented as Cases 3 and 14 in Dr. Sosman's comprehensive review published in 1957 (11).

In June 1956, an older sister of these patients was seen at Bucaramanga suffering from cor pulmonale. Roentgen examination of her chest showed pulmonary alveolar microlithiasis in a stage much more advanced than that in either of the two sisters previously observed. On that occasion, chest roentgenograms were also taken of a fourth sister, the youngest, who was apparently in good health. She too was found to have pulmonary alveolar microlithiasis. The oldest sister, who had a cor pulmonale, died in July 1957 and an autopsy was performed (see Case IV, below). The chest roentgenograms of a fifth sister, who was married and lived elsewhere, and those of a brother, who had also left home, were normal.

CLINICAL STUDY

History of the Family: The father of these four patients died in 1943 of peritonitis, at the age of seventy-two years. He had never had a chest roentgenogram. He is survived by two step-brothers who enjoy good health and were not examined. The mother of the patients died in 1935, at the age of fifty-eight, of anemia due to metrorrhagia. She had not at any time had a chest roentgenogram. She had no surviving brothers or sisters.

This couple had lived throughout their married life in a rural house in La Mesa de los Santos, near Bucaramanga, Santander. The town lies on a plateau 1,700 meters above sea level and has a constant, pleasant climate, with temperatures between 18 and 20° C. The soil is arid and the vegetation scanty. Drinking water is obtained from springs in the town. There are numerous mines in the vicinity, some in actual operation, yielding calcium, kaolin, iron, and baryta.

The couple had seven children (five girls and two boys), all of whom were born in the same house. The oldest son died in 1931 from a cerebral hemorrhage at the age of thirty-two years. During his life he had not had a chest roentgenogram. As already stated, four of the sisters had pulmonary alveolar microlithiasis. Three of these are living at the present time, forty-nine, forty-seven, and forty-two years old, respectively. The second brother is fifty-four years old, in good health, and roentgenologically normal. He is married and has seven children on whom no roentgenograms have been obtained. The fifth sister is forty-three years old and is married but has no children. The four patients, in-

Fig. 1. Case I (E. A.). Roentgenogram of the chest taken June 28, 1948. Innumerable calcific particles, the size of grains of sand, throughout both pulmonary fields, but most marked in the bases.

cluding the one who died, have always lived in the home of their parents.

CASE I: E. A. was 40 years of age in 1948, when chest roentgenograms led to the discovery of pulmonary disease. She had lived all her life in a house by the side of a dusty road, not asphalted and carrying heavy traffic. Twelve years before her examination, the patient had experienced acute abdominal pain interpreted as renal colic because of associated moderate hematuria. Since that attack she had occasionally suffered from abdominal pain. Her appetite was fair. She did not cough nor was she unduly fatigued. She had never worked in any industries or in the mines. Her menstruation was normal. She had lost some weight during the last few years.

Roentgen Examinations: Roentgenograms taken at the first examination showed innumerable shadows of calcific density, the size of grains of sand, uniformly distributed throughout both pulmonary fields from the apexes to the bases. The minor interlobar fissure of the right side was thickened. Linear streaks, starting from the hili, extended radially, especially in the right upper lobe, reaching in some cases as far as the periphery of the lungs. These streaks appeared to be formed by calcific deposits along the blood vessels and the bronchi. The heart outlines were almost entirely effaced by the dense pulmonary process. The diaphragm shadows were completely obscured. There were calcific deposits on the walls of the aortic arch. The calcifications in the bases of the lungs and the calcific streaks along the pulmonary blood vessels could be distinguished through the gastric air bubble (Figs. 1 and 2).

In the second roentgen examination, in April 1956 (the patient at that time was forty-eight years

Fig. 2. Case I (E. A.). Right lung with higher magnification. The calcific deposits are arranged in streaks along the pulmonary blood vessels. Thickening of the minor interlobar fissure.

old), the lower half of the pulmonary fields appeared almost entirely obscured. Only in the upper portions was a little air visible among the typical concrements of microlithiasis. These concrements were more closely grouped and much more numerous than at the first examination. The pathologic process was more apparent on the right than on the left side. There was a clear zone, 2 cm. in diameter, from the region of the bifurcation of the trachea down to the base, in which there were no calcific deposits. The involvement of the lungs was undoubtedly more massive than in 1948 (Fig. 3).

Clinically the patient was apparently normal, except for the presence of a uterine fibroma which caused no symptoms. The roentgenograms of the urinary apparatus were negative for lithiasis.

Laboratory Data: Urine: specific gravity 1.020; *p*H 5; no albumin or sugar. *Blood:* serum calcium 4.9 mg. per cent (normal 4.2–5.1); cholesterol 190 mg. per cent; fasting blood sugar 80 mg. per cent; nonprotein nitrogen 31.2 mg. per cent; red cell count 5,600,000; hemoglobin 15.7 gm. (108 per cent); hematocrit 54 per cent; white cell count 8,000; differential count normal; sedimentation rate 39.0 mm. in one hour.

Course: A new clinical examination was made in July 1956, showing dyspnea on great exertion and

sometimes even on moderate exertion, with slight cyanosis of the lips, ears, and fingers.

In January 1957 the patient had a hysterectomy because of the uterine fibroma. The operation was well tolerated. Electrocardiograms taken in July 1956 and January 1957 were practically identical, both being within normal limits. The only electrocardiographic abnormalities found were high and acuminate P waves in D II and in D III and a left deviation of the AQRS (Fig. 4).

The carotid pulse was rhythmic, equal, and of normal intensity with a rate of 75 per minute. The blood pressure was 140/85. Cardiac sounds were normal, as was auscultation of the thorax. The apex of the heart was neither visible nor palpable. The patient was still dyspneic on exertion.

CASE II: In T. A., an unmarried woman aged 46, the disease was detected during a roentgen examination of the chest in April 1956. The patient had had typhoid fever in 1931 and acute appendicitis in 1952. She complained of frequent attacks of migraine headaches, but on physical examination appeared to be in normal health.

Laboratory Data: Urine: specific gravity 1.010; pH 5.5; no sugar or albumin; urate crystals 2+ in sediment. *Blood:* cholesterol 150 mg. per cent; nonprotein nitrogen 28.6 mg. per cent; red cell count 5,300,000; hemoglobin 14.5 gm. (100 per cent); hematocrit 50 per cent; white cell count and differential normal; fasting sugar 90 mg. per cent; Ca 4.8 mg. per cent (normal: 4.2–5.1); sedimentation rate 30 mm. in one hour.

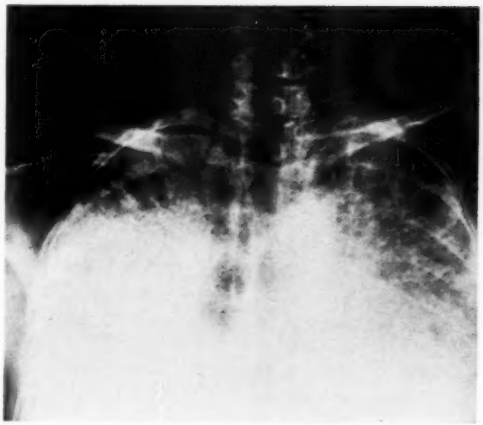


Fig. 3. Case I (E. A.). Roentgenogram of the chest taken in April 1956, eight years after the first roentgenogram, revealing marked progression of the lesions though the patient was still without symptoms.

Roentgen Examinations: The chest roentgenograms revealed a diffuse, finely mottled density

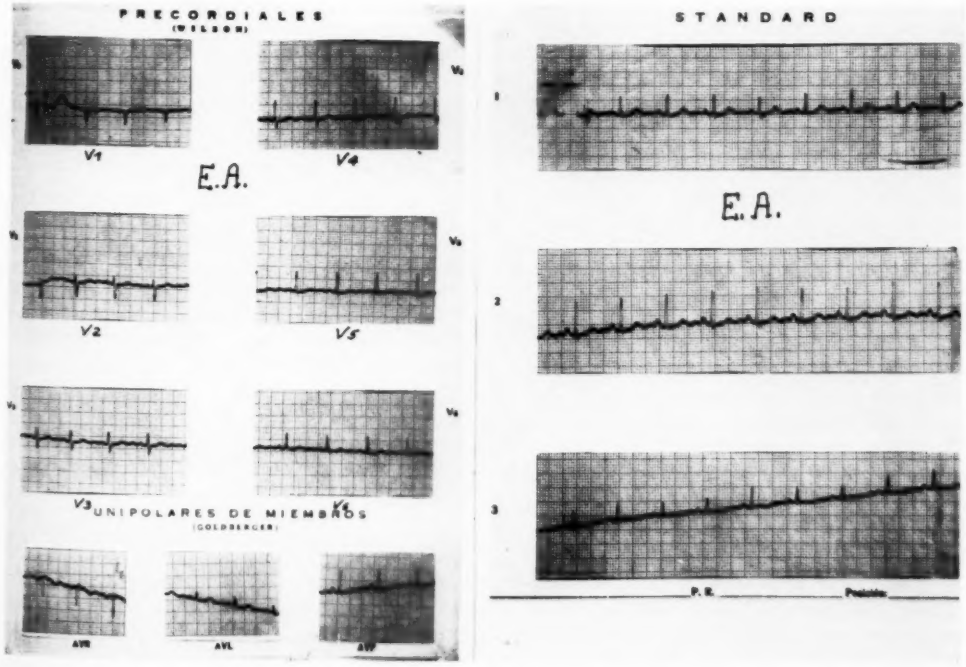


Fig. 4. Case I (E. A.). Electrocardiogram within normal limits but with high and acuminate P waves in D II and D III and deviation of AQRS to the left.

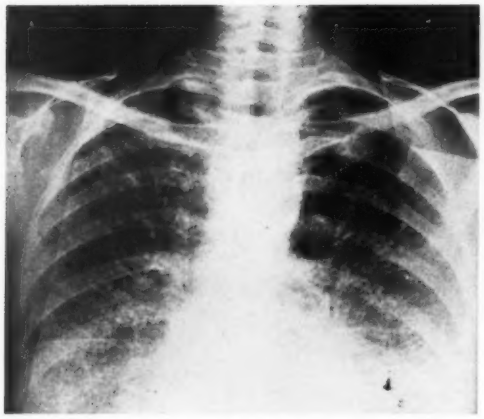


Fig. 5. Case II (T. A.). Roentgenogram of the chest taken in April 1956. Lesions slightly less advanced than those in Case I in 1948 (Fig. 1). Thickening of the minor interlobar fissure.

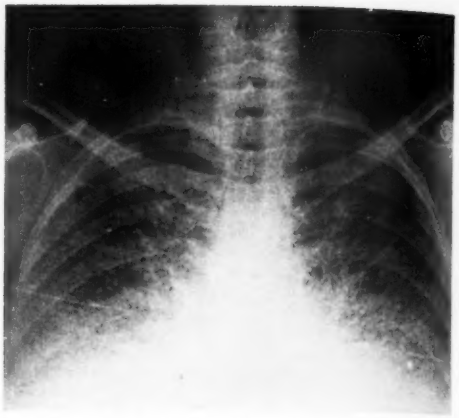


Fig. 6. Case III (M. A.). Roentgenogram of the chest taken in July 1956. Typical roentgen appearance of microlithiasis, slightly more advanced than in Case II. Thickening of the minor interlobar fissure.

throughout both lungs, from the apexes to the bases, most marked in the lower medial portions. Here the density was so great that the cardiac outlines and the diaphragm were completely obscured. The lungs, dense and calcified, could be seen through the upper abdominal shadow, with the normal vascular tree completely obliterated. The aortic knob was indistinct. Both upper lobes showed a fine reticulated pattern between the individual calcific granules. The bones retained their normal density and normal anatomic details. Roentgenologically, this was a case of pulmonary alveolar microlithiasis in an advanced stage. As in Case I, the minor interlobar fissure was thickened (Fig. 5).

New roentgenograms, taken in July 1957, showed no changes in the roentgen picture. Clinical examination at this time showed the patient to be alert, with dyspnea and cyanosis slightly less marked than before. The pulse was 80 beats per minute. Cardiopulmonary auscultation showed no abnormalities. The blood pressure was 130/80. A plain roentgenogram of the abdomen revealed no evidence of urinary calculi. The electrocardiogram was similar to that in Case I.

CASE III: M. A., an unmarried woman aged 41, gave a history of an appendectomy and phlebitis of the left leg, seven years earlier. Pulmonary alveolar microlithiasis was discovered by roentgen examination in July 1956. The patient complained of neuralgic pains in the back but had no other subjective symptoms. Neither cyanosis nor dyspnea was present. The pulse was 100 beats per minute, rhythmic, equal, and of normal intensity. Cardiac sounds were normal. Auscultation, palpation, and percussion of the thorax failed to reveal any abnormalities.

Electrocardiograms, taken in 1957, can be regarded as normal except for the fact that they show high and acuminate P waves in D II and D III and also a deviation of the AQRS to the left, similar to that associated with the much more advanced disease in Case I.

In a second clinical examination, dyspnea accompanying great exertion and cyanosis were encountered. These conditions were slightly more marked than at this time in Case I, which was roentgenologically much further advanced.

Roentgen examination showed the classic appearance of pulmonary alveolar microlithiasis in an advanced stage, with innumerable minute round or oval calcific granules distributed over the entire extent of the pulmonary fields, but in greater concentration in the lower halves. The opacity of the bases was so intense that the outlines of the diaphragm and the contours of the heart could not be distinguished. A series of divergent arborizations, which originated in the hilus and were surrounded by minute concrements, extended toward the periphery of the lungs. The aortic knob could not be distinguished. There was also pleuritis of the minor interlobar fissure (Fig. 6). In this case the disease was a little more advanced than in Case II.

CASE IV: I. A., an unmarried woman aged 50, had been treated for cardiac insufficiency at various times in the six years previous to her first roentgen examination in June 1956. In her first clinical examination she was told that she had hypertension.

The patient had had dyspnea for the last ten years. At first, it accompanied great exertion, but later changed progressively, becoming dyspnea on decubitus two years before the examination in 1956. Cyanosis had also been obvious for the last two years. There was precordial pain, usually related to exertion, but sometimes appearing spontaneously. On most occasions, it radiated to the back, the neck, and the left shoulder and lasted only a few minutes.

Occasionally, however, it continued for about half an hour and was associated with a sensation of anguish. Edema of the ankles, occurring in the evening, had appeared for the first time six years earlier, disappeared with treatment, but then had become permanent. Other complaints were: headaches, without fixed hours; cough, either dry or with scanty sputum of the mucous type, more severe at night, during decubitus; dysuria; diminution of total quantity of urine. Menstruation was normal.

The patient had had herpes zoster when she was twenty years old and again five years before her examination; she had had erysipelas on the right leg seven years earlier.

Examination showed severe cyanosis, with dyspnea which increased with talking. The patient was alert and optimistic. When she was semi-seated the jugular veins were dilated. The carotid pulse was rhythmic and equal, 110 beats per minute. The lower part of the anterior portion of the thorax was prominent and round. The anterior part of the lower ribs appeared to project forward.

The cardiac cycle was rhythmic, with presystolic gallop rhythm. The second sound was accentuated in the second left intercostal space. A small systolic blowing phenomenon was audible at the apex, occurring in midsystole. This did not efface any sound, and did not radiate. There was cyanosis of the fingers but no evidence of clubbing. The liver was palpable two fingers below the costal border in the clavicular midline, and was painful. Edema in the lower limbs reached up to the knees. The blood pressure was 140/90.

Treatment was by digitalis, Diamox, and Davasal. Digitalization was continued until death.

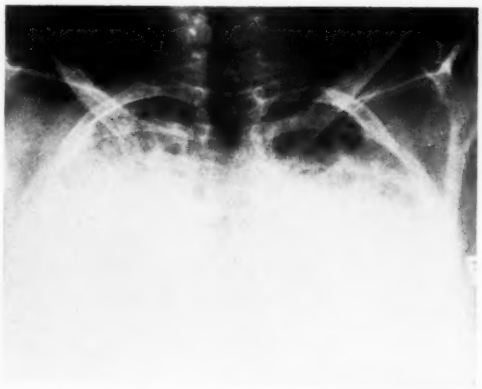


Fig. 7. Case IV (I. A.). Roentgenogram of the chest taken in June 1956, one year before death. The calcific deposits are visible only in the first two intercostal spaces on the right side and the first three intercostal spaces on the left side. The opacity is complete and uniform throughout the rest of the pulmonary fields and therefore the heart outlines cannot be seen.

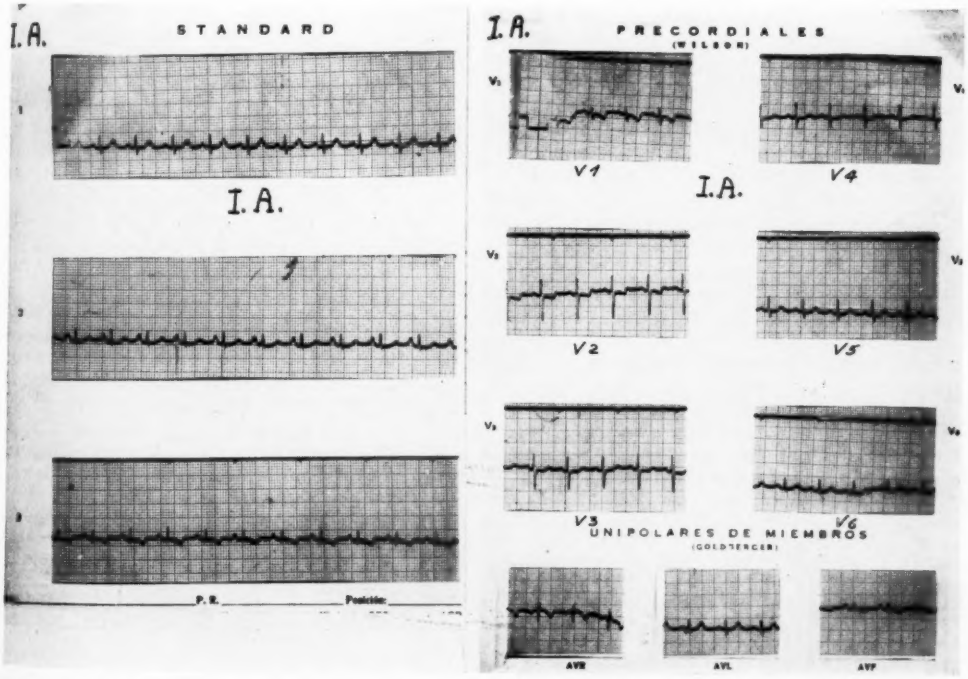
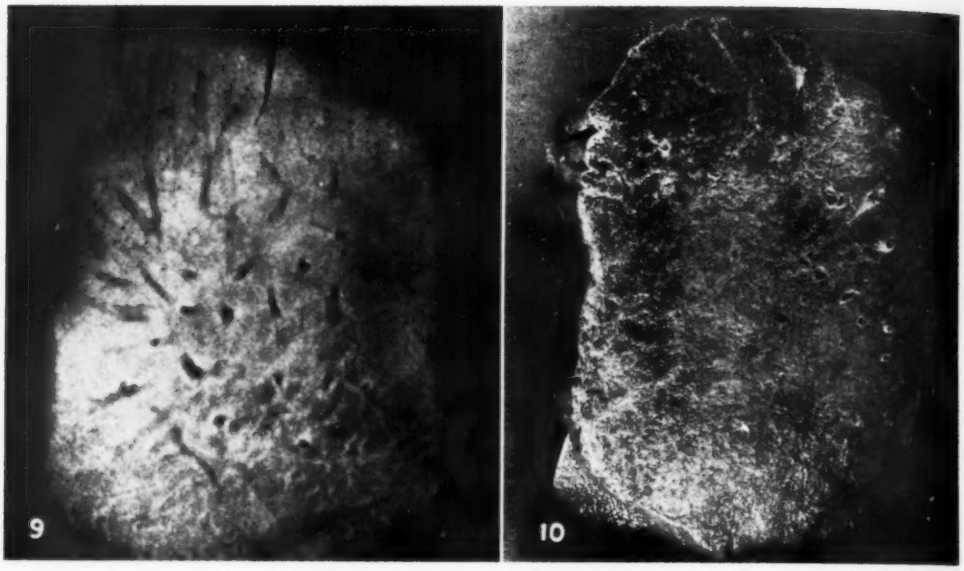


Fig. 8. Case IV (I. A.). Electrocardiogram which corroborates the diagnosis of cor pulmonale.



Figs. 9 and 10. Case IV (I. A.). Autopsy specimen of left lung: roentgenogram (Fig. 9) and cut surface (Fig. 10)

Roentgen Examination: The lower three-fourths of the hemithorax were completely obscured and the outlines of the diaphragm and the cardio-aortic silhouette could not be seen, nor were calcifications visible. Only at the apexes and in the infraclavicular zones were innumerable minute concrements, the size of grains of sand, to be seen, more clearly on the right side than on the left. The trachea and its bifurcation were quite distinct. The pleura was markedly thickened, 2 mm. in the upper external part on both sides, but especially on the right. The visible concrements were radiologically typical of microlithiasis. The bones appeared quite normal (Fig. 7).

It was on the occasion of this examination that a diagnosis was made of cor pulmonale with cardiac insufficiency from venous congestion and coronary insufficiency, in addition to pulmonary alveolar microlithiasis. The electrocardiogram confirmed the diagnosis of cor pulmonale. There was a deviation of the AQRS (+80) to the right (Fig. 8).

A little later the patient contracted grippe, which, however, caused no aggravation of her general condition. Administration of Meticortelone, in daily doses of 15 mg., was continued for a month without causing any improvement or aggravation of the clinical symptoms.

In July 1957, the patient suddenly became worse and for seven days was in a critical condition, having constantly to breathe from an oxygen mask, because of asphyxia and cyanosis. Most certainly, this final episode was caused by thrombosis of one of the branches of the pulmonary artery and the pulmonary infarction which was found at autopsy.

Anatomicopathologic Study: For the anatomicopathologic study, fragments of the heart and of the lungs were sent to two laboratories: the laboratory of the Institute of Pathologic Anatomy of the Faculty of Medicine of the University of Antioquía and the laboratory of the Department of Pathologic Anatomy of the San Juan de Dios Hospital, of Bogotá. For convenience, the reports are combined in this article.

In general, a marked hypertrophy of the *heart*, especially of the right chambers, was observed. The right ventricle measured 0.7 cm. in thickness (normal 0.2 to 0.3 cm.); the left ventricle 1.5 cm. (normal 0.8 to 1 cm.). The circumference of the pulmonary ring was 6.5 cm. (normal 8.5 cm.). The papillary muscles were also thickened and hypertrophic. The leaflets of the valves were, in general, normal, except those of the mitral valve, which were thickened at the edges. The myocardium was firm and pale. The parietal endocardium did not show any changes. The epicardium of the posterior surface showed a plaque of pearly white color which measured 2 cm. in its greatest diameter. The coronary arteries contained a small number of atheromatous plaques but the arterial lumen was not reduced.

Both *lungs* were of normal size but of greatly increased weight. The right lung weighed 630 gm. (normal 360 to 570 gm.); the left lung 598 gm. (normal 325 to 480 gm.). Externally, there was hemorrhagic mottling of the pleura with some remains of adhesions, especially toward the apexes. Upon palpation a great increase in consistency was strikingly noticeable, together with a diminution of crepitation, which was partially preserved only in the

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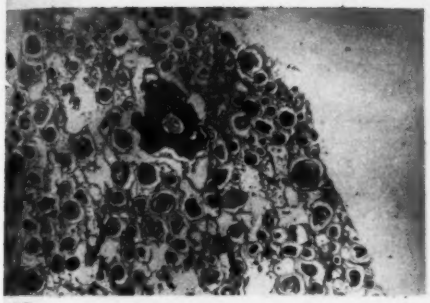

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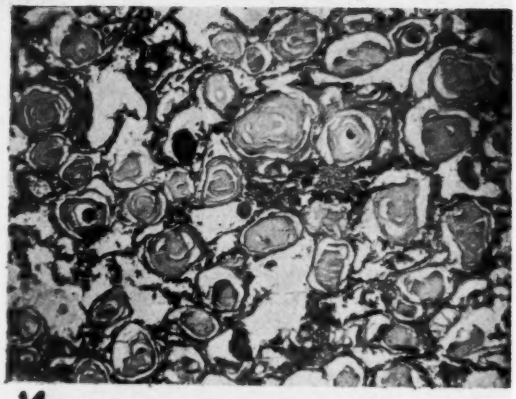

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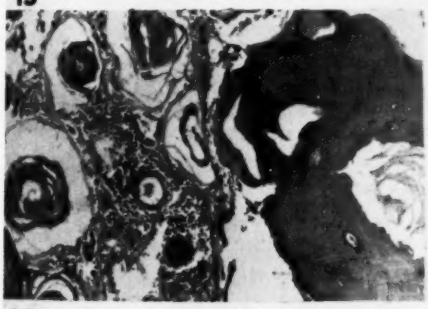

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Figs. 11–16. Case IV (I. A.). Microscopic sections (autopsy). Fig. 11. Cut surface of left lung. Fig. 12. Myocardium, showing hypertrophic muscular fibers. × *c*.95. Fig. 13. Microliths and osseous tissue in lung × *c*.45. Fig. 14. Calcospherites and stroma with moderate mononuclear infiltration. × *c*.95. Fig. 15. Microliths and osseous tissue. × *c*.95. Fig. 16. Calcospherite under high magnification. × *c*.650.

upper lobes. On section, the parenchyma showed a homogeneous aspect. It was yellowish-pink and very firm. When it was cut, one had the impression of passing the knife over sandpaper, and the presence of innumerable granules, suggesting fine grains of sand, became discernible (Figs. 9–11). The pulmonary arteries showed some thrombi in process of organization. A triangular hemorrhagic zone, 2.5 cm. in diameter, which seemed to be a small infarct, was visible in the left lower lobe. The arterial walls were slightly thickened and presented some atheromatous plaques. The bronchi showed no changes. In the hilus of the right lung, small anthracotic nodes were encountered.

Microscopic Description: The fibers of the *myocardium*, especially those of the right ventricle, showed hypertrophy of a severe degree (Fig. 12). In addition, they contained an abundant amount of waste pigment. There were interstitial edema and a slight increase in the connective tissue which,

in spots, was infiltrated by a small number of mononuclear inflammatory cells. Congestion and hypertrophy of the walls of some arteries of small caliber were observed. There was no evidence of rheumatic fever, although sections of the mitral valves showed foci of fibrinoid necrosis of the collagen. The walls of the right coronary artery were thickened; the artery contained lipophagic cells and there were small capillary spaces with foci of interstitial hemorrhage in its middle layer.

Sections of the *lungs*, made at different sites, all showed the classical picture of alveolar microlithiasis (8, 11–14). Practically all the alveoli were filled with concrements composed of concentric layers of material of calcific appearance (Figs. 13–16). These concrements were of various sizes and were almost always free within the alveolar lumen, although this appearance could have been due to a defect in the preparation; there were places in which the microliths or calcospherites were found in close contact with the alveolar wall. There were also osseous formations with dentate borders, consisting of osseous substance of the usual architecture (Figs. 13 and 15). Occasionally, some of these formations enclosed one or several microliths. The alveolar lining was, in general, smooth but many of the alveolar walls themselves were thickened as a result of the increase in the fibrous connective tissue. In some of the alveoli, not occupied by microliths, there were squamous cells having the appearance of macrophages and even some multinuclear giant cells. The blood vessels and capillaries were engorged with blood. One section showed a thrombus in process of organization in a branch of the pulmonary artery of medium caliber. Another section showed a zone of infarction of the parenchyma with partial destruction of the alveolar walls. The bronchi were found to have normal characteristics. The walls of the smaller pulmonary arteries were only slightly thickened. There was no evidence of inflammation, although a few accumulations of lymphoid cells were observed. The pleurae were slightly thickened, with marked subpleural congestion.

Diagnosis: Bilateral pulmonary alveolar microlithiasis; thrombosis of a branch of the left pulmonary artery of medium caliber; left pulmonary infarct (small); hypertrophy of the heart, especially the right heart (chronic cor pulmonale).

COMMENTS

The chest roentgenograms in the four cases reported above closely resemble those described in earlier accounts of alveolar microlithiasis. In three of the sisters, a pleural thickening over the minor interlobar fissure was a constant roentgen finding. Whether or not this feature was present in the oldest sister (the one who died) cannot be stated definitely, since roentgenographically the lower three-fourths of her lungs were completely opaque. The autopsy findings were in perfect agreement with the anatomic and histologic descriptions previously given of the disease (8, 11–14).

The discovery of alveolar microlithiasis in four sisters corroborates once more its familial occurrence. Up to the present time seven instances of familial occurrence of microlithiasis have been reported in the literature (9–11). They include: Three instances in which the disease occurred in three members of a single family, two of them in brothers, and one in a brother, his sister, and her son; two instances in which it occurred in two brothers; and one in which it occurred in a family of four sisters. The present report describes a second group of four sisters. The 23 cases of this disease published by Dr. Sosman and collaborators (including 2 of our cases), the 22 cases previously reported in the literature, and our 2 additional cases, make a total of 47 examples of familial microlithiasis, of which 21 were in men and 26 in women.

In the 4 cases presented in this report, the most advanced lesions were observed in the oldest patient. Second in severity were the lesions in the next oldest patient. In the two younger sisters, the pulmonary lesions were less advanced. They were more marked, however, in the younger of the two. It cannot be stated, therefore, that, as might be supposed, the disease appears at approximately the same age. The patient who is only two years younger than the oldest patient had, in 1956, a chest roentgenogram very similar to that presented by her older sister in 1948.

The disease was discovered in these four women when they were forty, forty-one, forty-six, and fifty years old, respectively, just as most of the cases in the literature have been found in patients between the ages of thirty-one and fifty years. It should be recalled, however, that cases of the disease in children of six, eight, ten, and twelve years of age, who were still asympto-

matic, have been reported (10, 11, 16, 17).

The lack or near lack of symptoms in patients with pulmonary alveolar microlithiasis in the presence of strikingly advanced lesions demonstrable roentgenographically is corroborated in the three surviving patients of this report. On Oct. 19, 1957, when we last saw them, we found them, to our surprise, in a condition of health which was in complete disagreement with their chest roentgenograms. Two of the sisters, including the one in whom the disease was most advanced (Case I) walked briskly without exhibiting dyspnea or cyanosis of the face or hands. Only the youngest patient, whose pulmonary lesions were less advanced than those of the first patient, had dyspnea on moderate exertion and moderate cyanosis.

Thus, the external appearance did not correspond to the extent of the pulmonary lesions. It was noticed that the two sisters who were in a better condition of health were thinner than the one who exhibited some symptoms. The constitution of this latter patient—with a tendency to obesity—was similar to that of the patient who died after having suffered with dyspnea and cyanosis for several years.

We wish to emphasize the fact that none of these three patients has cough or has ever complained of coughing. We emphasize this fact because we believe that cough is not a symptom of uncomplicated alveolar microlithiasis, and that it appears only when cor pulmonale supervenes, as in Case IV, or in the presence of some associated bronchopulmonary disease.

The electrocardiographic studies showed that from the very beginning of the disease there is damage to the myocardium, indicated by the appearance of changes in the P waves of the electrocardiogram. The myocardial involvement is of obscure etiology. At first sight it would be natural to expect a marked hypertension of the lesser circulation, of a systolic type, with a notable increase in the second pulmonary sound, a deviation of the AQRS to the right, high R waves in lead V and a deep S in lead VI, with consequent changes in S-T and T. By contrast, the electrocardiograms of the three surviving patients showed a left electric axis and precordial leads that were practically normal (Fig. 4); that of the fourth patient, who already had evident cor pulmonale, was different (Fig. 8). The P waves corresponded in form to those which have been described in electrocardiograms showing diminution of oxygen saturation of the blood to below 71 per cent and, less frequently, when the right ventricular systolic tension reaches or rises above 130 mm. Hg, as described by Peñaloza and collaborators of Mexico.

The question that remains is whether pulmonary microlithiasis, besides having a familial nature, may be due to a second unknown factor, found in the environment, which favors its development in the organism of a person previously predisposed to it. This possibility is suggested by the fact that our four patients with the disease—"stony lung," as the people of this region call it—were born and lived all their lives in the same house in the same place and locality, with the same environment and the same diet, while the brother who left the family home in 1923 when he was twenty years old, and the sister who left home in 1916 at the age of two years, are not affected. On the other hand, roentgen examinations of numerous other people living in the same region, some in the same house with the patients, showed no evidence of microlithiasis.

The water from the well from which the patients have always obtained their drinking water was examined before and after filtration and was not found to contain any constituent which could be considered harmful to the health of its consumers. The results of analyses of the drinking water were as follows:

	Sample(1) Natural		Sample(2) Filtered	
*p*H value	7.0		8.0	
Phenol alkalinity ($CaCo_3$)	0.0	mg./lt.	0.0	mg./lt.
Total alkalinity ($CaCo_3$)	12	"	45	"
Free content of carbon dioxide (CO_2)	2.5	"	1.0	"

Total hardness ($CaCO_3$)	2.3	"	2.8	"
Calcium (Ca)	0.9	"	1.0	"
Magnesium (Mg)	0.02	"	0.07	"
Total iron (Fe)	1.4	"	0.1	"
Bicarbonates (HCO_3)	15	"	55	"
Carbonates (CO_3)	0.0	"	0.0	"
Chlorides (Cl)	5.0	"	5.0	"
Sulphates (SO_4)	1.2	"	1.2	"
Nitrates (NO_3)	0.16	"	0.18	"

These results indicate that the natural water of the well has a neutral reaction with relatively low total alkalinity and that it can be classified as being very soft. In addition, except for a slight excess of iron, it can be said to have an extremely low total mineral content, since the concentration of each of the other elements and salts is practically insignificant. These properties of the water give it a very marked dissolving power.

With regard to the filtered water, it may be seen that, apart from improvement in physical appearance after filtration, there is a marked increase in the alkalinity and the *p*H, produced, possibly, through a dissolving action on the filter material and a consequent reduction of iron hydrates, all of which result in considerable improvement of the water for drinking purposes.

SUMMARY

1. Four cases of familial pulmonary alveolar microlithiasis, the first cases to be discovered in Colombia, S. A., are reported. One of the patients died and an autopsy was performed. The patients were four sisters in a family of seven children (two boys and five girls).

2. The results of roentgen and clinical studies, the course of the disease, and the anatomicopathologic studies are in accord with reports in the literature.

3. Attention is directed to the frequent presence of a pleural thickening over the minor interlobar fissure, and to the absence of cough, so long as cor pulmonale does not supervene.

4. In the final stages of the disease, the roentgen image is that of cor pulmonale. During the very long period of development, the electrocardiographic tracings do not show definite myocardial damage in the ventricular complexes, except for a highly questionable blockage of the bundle of His. By contrast, in the auricular complex, relatively high acuminate P waves were observed in D II and in D III, at least in the electrocardiograms of two of the patients. The electrocardiograms of all the patients, with the exception of the one who had cor pulmonale, showed the AQRS nearer to 0° than to 90°.

5. The earliest manifestations of the disease are dyspnea and cyanosis which, however, are not proportionate to the severity of the lesions as demonstrated roentgenologically. In some cases these symptoms appear relatively early, whereas in others they may be almost nonexistent even though the lesions are far advanced.

6. The possibility that microlithiasis may not be exclusively familial but that environmental and dietetic factors may play a role in its onset, in persons previously predisposed, is suggested.

7. So characteristic is the roentgen appearance that the roentgenologist who has once seen a chest film of one of these patients and who keeps in mind the paucity of symptoms, can make the diagnosis of microlithiasis with certainty, without waiting for histologic confirmation.

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SUMMARIO IN INTERLINGUA

Familial Microlithiasis Pulmono-Alveolar: Quatro Casos Ab Colombia, Sud-America

Es reportate quatro casos de familial microlithiasis pulmono-alveolar que es le primes unquam discoperite in Colombia, Sud-America. Le patientes esseva quatro sorores inter septe fraternos, duo pueros e cinque pueras. Le diagnose esseva primo establite quando le etates del patientes esseva 40, 41, 46, e 50 annos, respectivemente. Un del patientes moriva, e un necropsia esseva effectuate.

Le resultatos del studios roentgenologic e clinic, le curso del morbo, e le studios anatomico-pathologic es de accordo con le reportos in le litteratura.

Es signalate le frequente presentia de un spissification pleural supra le minor fissura interlobar e le absentia de tusse (excepte quando corde pulmonal ha supervenite).

In le stadios final del morbo, le roentgenogramma es illo de corde pulmonal. Durante le prolongatissime disveloppamento del morbo, le electrocardiogramma non monstra definitemente le presentia de lesiones myocardial in le complexos ventricular, con le exception de un multo questionabile blocage del fasce de His. Per contrasto con isto, in le complexo auricular le presentia de relativemente alte e acuminate undas P esseva notate in D II e in D III, al minus in duo del casos. Le electrocardiogrammas de omne le patientes, con le exception de ille qui habeva corde pulmonal, monstrava le complexo AQRS plus proxime a 0 que a 90°.

Le prime manifestationes del morbo es dyspnea e cyanosis, sed istos non es proportional al severitate del lesiones in le roentgenogramma.

In certe casos iste symptomas se manifesta relativemente tosto, durante que in alteres illos pote remaner quasi nonexistente in despecto del facto que le lesiones es jam multo avantiate.

Es suggerite le possibilitate que microlithiasis non es exclusivemente familial sed que in personas susceptibile, factores ambiental e dietari ha un rolo in le declaration del morbo.

Le apparentia roentgenologic del morbo es si characteristic que le roentgenologo qui ha vidite un sol roentgenogramma thoracic de un patiente con illo pote, providite que ille se rememora le paucitate del symptomas, establir le diagnose definitemente.

Upright Large Volume Dynamic Myelography[1]

BRUCE N. KVERNLAND, M.D., RAY V. GREWE, M.D., IVAN M. WOOLLEY, M.D., and J. ROBERT LEE, M.D.

THE USUAL PANTOPAQUE myelographic study, employing 6 or 9 c.c. of contrast material with the patient prone, in oblique and lateral projection, has long been recognized as inadequate in certain types of cases. Patients with undeniable neurologic changes in the lower extremities have too frequently been declared free from evidence of pathology because the opaque myelographic study failed to reveal the defect.

The neural canal is a three-dimensional structure and therefore possesses a posterior surface as well as anterior and lateral margins. Pantopaque, being heavier than the spinal fluid, settles to the most dependent areas, which, when the patient is in prone position, are along the anterior surface. In some instances, a lateral radiograph taken across the table will show some of the posterior surface outlines, but this is not so in every case.

The spine is a dynamic structure and the configuration of the spinal canal changes with bending. It is to be expected that, when the spine is carrying weight, certain pressures may develop that may disappear when the weight is removed.

Patients with increased lumbar lordosis frequently suffer low-back pain and pain in the legs upon becoming fatigued. Many observers beside ourselves have long suspected that these symptoms arise from actual pathological changes that we have failed to demonstrate because we did not visualize the neural canal in all of its three dimensions. Grayson and Black (4), as well as many others (1, 2, 6), recognized these deficiencies and made considerable progress towards eliminating them by increasing the amount of contrast substance in order to fill the subarachnoid space more completely. The effect of motion upon the contours of the canal was considered by Bell *et al.* (1) and Brierre and Colclough (2), who instituted large-volume studies with weight-bearing. Attempts were made to visualize disk lesions after bending movements, but it is our understanding that the bending was done prior to radiography and was not maintained during film exposure.

Having encountered numerous baffling failures in demonstrating lesions that we knew must be present, we have attempted to combine various factors needed to visualize all the surfaces of the canal with the patient in prone, oblique, and upright weight-bearing positions, together with upright lateral projections taken with the spine in flexion and in extension. It is our practice to employ this technic with patients who display definite cauda equina type symptoms that can be supported by the history and physical findings. Included in this group are those who have obtained a solid surgical fusion of L-4, L-5, and the sacrum without relief of symptoms and at times with an increase in neurological deficit. Also included are those in whom fusion is not solid and symptoms persist. Neurologic examination of this group demonstrates evidence suggestive of some mechanical impingement upon the cauda equina, either constant or intermittent. We have found that it is worthwhile also to check those patients with persisting symptoms in whom adequate evidence was not obtained by the use of routine prone Pantopaque studies.

It is our practice to give the patient a mild sedative prior to bringing him to the x-ray department. We have found that 1 grain of codeine plus 1 grain of Luminal Sodium, hypodermically, produces satisfactory relaxation. The lower extremities are wrapped with elastic tensor bandages to minimize the danger of vascular hypo-

[1] From the Neurosurgical Service and the Department of Radiology, Emanuel Hospital, Portland, Ore. Presented at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

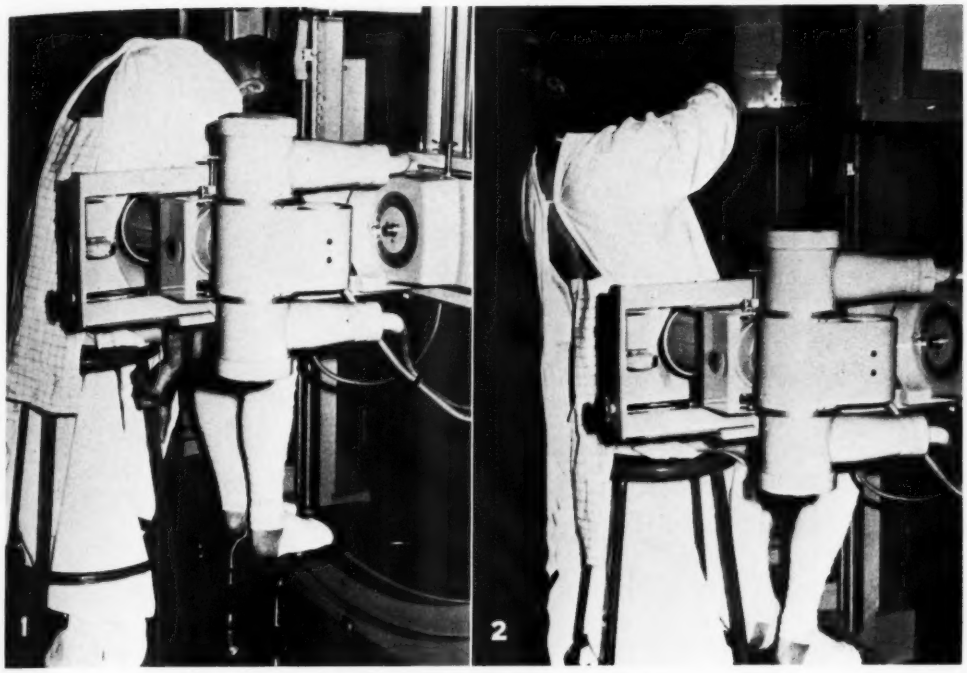


Fig. 1. Patient in position with spine flexed.
Fig. 2. Patient in position with spine hyperextended.

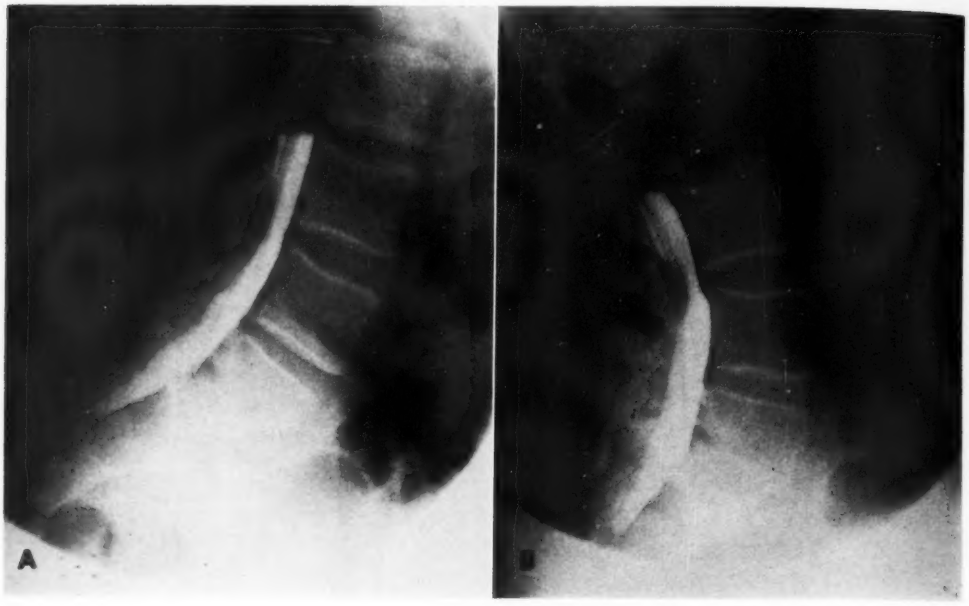
tension when a change is made from prone to upright position.

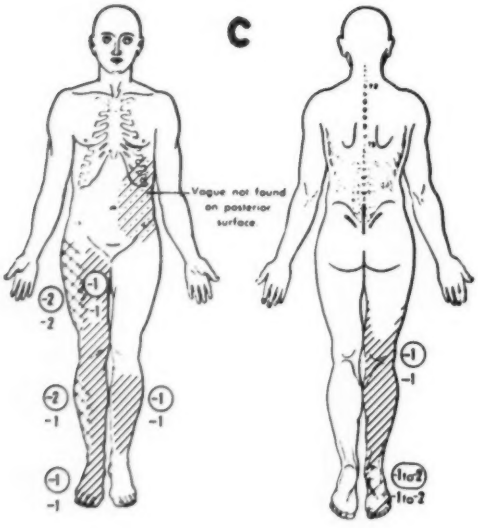
The patient is placed prone upon the radiographic table with the footboard securely in place. With the usual surgical precautions as to skin sterilization, draping, etc., the spinal puncture is made. For this we prefer an 18-gauge needle. In order to avoid needle artefact in the region under investigation, the puncture is made at a level above that of the suspected lesion, if possible. In no instance, however, should it be high enough to contact the conus medullaris. Following puncture, the usual tests of spinal fluid dynamics are carried out.

We prefer to observe the entrance of the first few drops of Pantopaque under the fluoroscope to make sure that the needle is adequately placed in the subarachnoid space. Satisfactory protection of the operator from radiation is provided by a small-lumen rubber or polyethylene tube approximately 16 inches in length, which transmits the Pantopaque from the syringe to the needle. With the patient's head somewhat elevated, the first few drops of contrast substance are observed to enter the subarachnoid space If all is satisfactory, the x-ray is turned off and the rest of the medium is instilled under usual light. After replacing the stylet in the needle, prone, oblique, and lateral studies are carried out.

If a large-volume dynamic study is indicated, a 12-c.c. ampule is opened and the Pantopaque is slowly added through the needle. The contrast level is checked from time to time by slowly raising the table until the patient is in a near-standing position. When the injection is adequate, the stylet is replaced in the needle, which remains *in situ*, and the patient is redraped, care being taken that the drapes are secure enough to remain in place in the upright position. If additional postero-anterior or oblique film studies seem desirable, they can be made at this time.

The table, equipped with Bucky diaphragm, is slowly elevated to vertical





SENSORY CODE

Vague		
−1	−25%	
−1 to −2	−25% to −50%	
−2	−50%	

(Circled Numbers Indicate Pain)

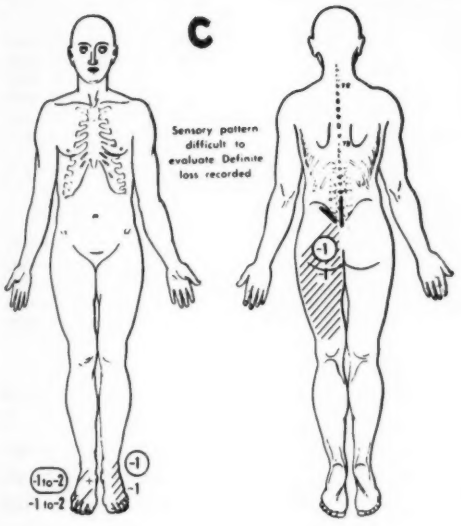
Fig. 3. Case I. Solid fusion of L4–5. Posterior defect at L3–4. History: Back injury, Oct. 9, 1953. Disk removal and low-back fusion, November 1954. Further fusion, November 1955. Jan. 28, 1958: Continued complaint of low-back, right hip, and coccygeal pain, with poor penile sensation and difficulty in obtaining erection.

A. Upright dynamic myelogram (15 c.c.), May 1, 1958, with spine flexed.

B. Upright dynamic myelogram (15 c.c.), May 1, 1958, with spine hyperextended.

C. Neurological summary chart. Examination, Jan. 28, 1958. Hyperextension of low back produces right groin and testicle pain. Reflexes normal except mild reduction of right knee jerk and moderate reduction of cremasteric reflexes bilaterally. Motor function considered normal.

position, which brings the patient to a standing position on the footboard. A tall stool is placed behind him and, properly assisted, he seats himself upon it. The footboard is then removed from the table and the stool is rotated to bring him into a true lateral position. An 11 × 14-inch cassette is placed in the Bucky tray and the x-ray tube is positioned at 40-inch tube-film distance. The patient now bends forward as far as possible in order to flex the spine, care being taken to prevent rotation of the pelvis anteriorly during the maneuver. He is then centered to the Bucky and the central beam from the tube is directed at the level of the



SENSORY CODE

Vague		
−1	−25%	
−1 to −2	−25% to −50%	
−2	−50%	

(Circled Numbers Indicate Pain)

Fig. 4. Case II. Solid fusion of L4–5, S1. Posterior defect at L3–4. History: Back injury, March 30, 1955, with severe low-back and left leg pain. Routine myelogram (prone) (9 c.c.) considered negative, Dec. 1, 1955. Decompression of roots of L4–5 and S1, June 7, 1956. Examination May 1, 1957: Pain persisted in lower back, and became bilateral to heels. Numbness of right foot and left foot and calf.

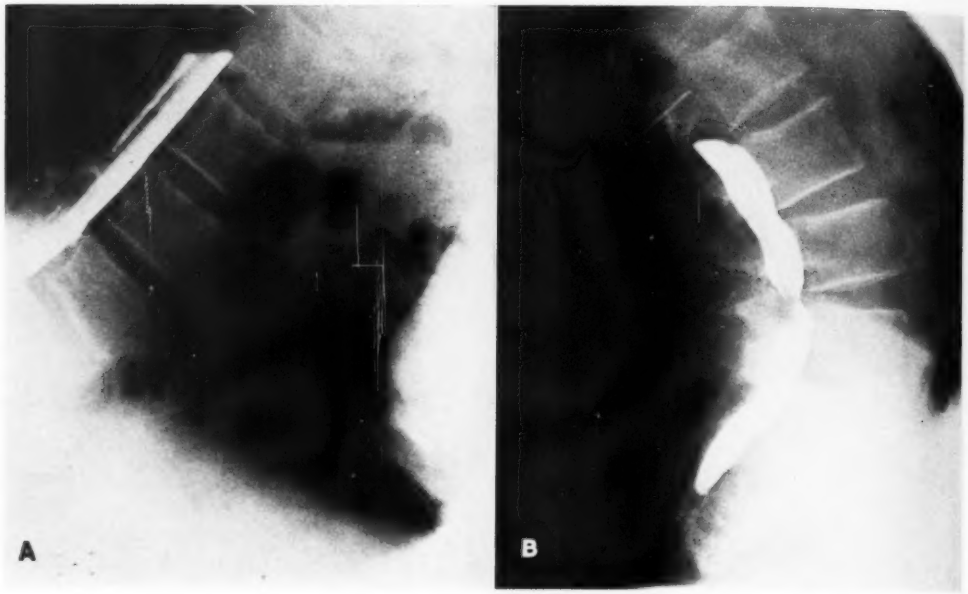
A. Upright dynamic myelogram (21 c.c.), May 14, 1957, with spine flexed.

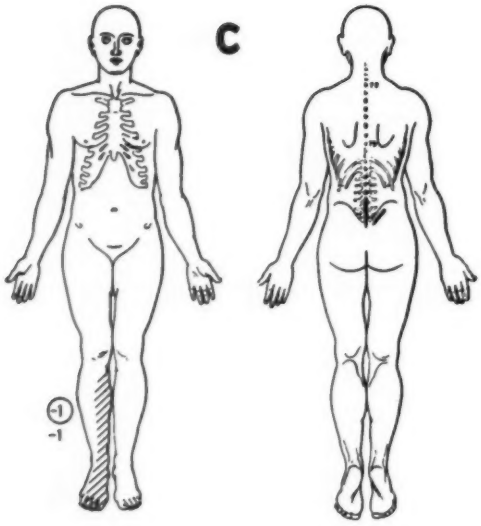
B. Upright dynamic myelogram (21 c.c.), May 14, 1957, with spine hyperextended.

C. Neurologic summary chart. Examination, May 1, 1957. Tender upper fusion mass. Hyperextension of low back markedly increases pain. Left knee jerk slightly less active than right. Right ankle jerk absent. Mild weakness of dorsiflexor of left large toe.

iliac crest. The first film is now exposed (Fig. 1). For the second exposure, the patient arches his back as far as possible. The centering is readjusted and the second exposure made (Fig. 2). During this maneuver, the patient steadies himself by grasping the edge of the table with one hand; with his other hand he holds firmly to the wrist of the anchor hand.

With the patient still seated, the stool is carefully shifted away from the table, the footboard is replaced, and the patient, properly assisted, steps upon it, again facing the table in upright position. The table is then slowly returned to a moderate Fowler's position. It is not returned to horizontal position because of the danger





SENSORY CODE

Vague		
−1	−25%	
−1 to −2	−25% to −50%	
−2	−50%	

(Circled Numbers Indicate Pain)

Fig. 5. Case III. Solid fusion of L5–S1, failure of fusion, L4–5. Posterior defect at L4–5. History: Back injury, September 1955. Conservative treatment with failure. Fusion, low back, Feb. 29, 1956. Patient improved until May 3, 1957. Cutting lawn led to severe recurrent pain in low back, with radiation into both legs; persistent.

A. Upright dynamic myelogram (18 c.c.), June 27, 1957, with spine flexed.

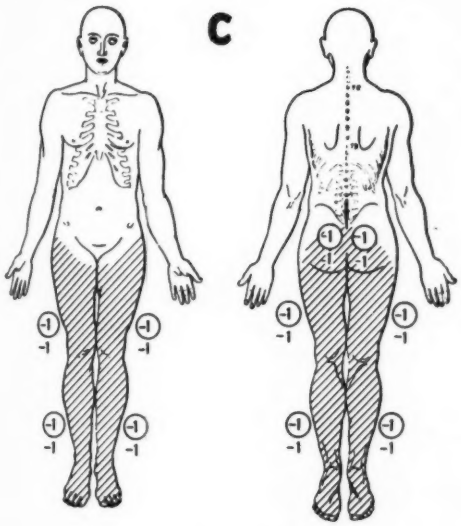
B. Upright dynamic myelogram (18 c.c.), June 27, 1957, with spine hyperextended.

C. Neurologic summary chart. Examination, June 14, 1957. Cephalic portion of fusion mass extremely tender. Hyperextension produces increased low-back pain. Mild reduction of right knee and ankle jerks. Motor function considered normal.

of the large volume of Pantopaque passing upward beyond the dorsal curve and entering the cranial cavity.

When it is ascertained that the films are satisfactory, the Pantopaque is withdrawn through the original needle or through a second needle placed at a lower level if this is thought to be more expeditious. If the needle is gently pushed to a depth approaching the anterior wall of the subarachnoid space, successful aspiration is more easily accomplished. The use of the tubing previously described makes it possible to recover the smaller residual droplets more quickly under fluoroscopic control.

The quantity of contrast material re-



SENSORY CODE

Vague		
−1	−25%	
−1 to −2	−25% to −50%	
−2	−50%	

(Circled Numbers Indicate Pain)

Fig. 6. Case IV. No fusion. Visible anterior and posterior defects at L3–4. History: Back injury, April 1950. Myelogram (3 c.c.) July 7, 1950, demonstrated defect at L3–4, left. Laminectomy, L3–4, left, showed minimal disk herniation; no fusion. June 16, 1957, complaint of spasms in low back, with pain radiation to posterior knees and large toes.

A. Upright dynamic myelogram (18 c.c.), June 24, 1957, with spine flexed.

B. Upright dynamic myelogram (18 c.c.), June 24, 1957, with spine hyperextended.

C. Neurologic summary chart. Examination, June 16, 1957. List of lumbar spine to right. Hyperextension of low back reproduces pain in low back and entire leg. Reflexes regarded as normal except for questionable reduction of knee jerks bilaterally. Plantar flexors of foot regarded 25 per cent lost on left; suggestive loss on right.

quired varies with each case. High lesions and large neural canals require more than other types. We have used as much as 36 c.c. in one case and as little as 12 c.c. in others. We have found that the average patient requires approximately 15 to 18 c.c. No untoward symptoms have been encountered in any of the patients thus far examined by this method, although no additional spinal fluid is removed.

These studies have provoked considerable interest concerning those patients in whom numbness of the feet and other evidences of cauda equina compression have developed. We find that this prob-

lem is more frequently present following successful fusion of L-4, L-5, and the sacrum than following successful fusion of only L-5 and the sacrum. We believe this to be due to the greater leverage applied to the midlumbar region as a result of the longer distal segment of the fused spine. In these cases we have been able to demonstrate impingement upon the posterior aspect of the column by the so-called cephalic ledge of the lamina and perhaps to some extent by the ligamentum flavum. The hyperextended attitude of the low back appears to produce a localized decrease in the anteroposterior diameter of the neural canal. Buckling of the annulus at times contributes to the decrease in anteroposterior diameter. Sometimes these two conditions can be demonstrated at the same level, producing a pincers-like encroachment upon the contrast column.

We have found Pantopaque (iophendylate injection U.S.P.) to be quite satisfactory for routine myelographic studies. We believe that a medium of lesser density would prove advantageous in the larger volume technic. The manufacturers are well aware of this problem and have been attempting to produce such a substance. We are most grateful to them for their unselfish assistance to us throughout these studies. We must also acknowledge the valuable assistance given this study by the orthopedic staffs of various hospitals and particularly the orthopedists of the Emanuel Hospital, Portland, Oregon.

SUMMARY

Encroachment upon the subarachnoid space from pathological processes arising posteriorly can be shown only when the posterior surface of the canal is visualized. Intermittent impingements brought about by weight-bearing and bending motions of the spine may be entirely missed in routine prone myelography.

A combination of upright, large-volume myelography with studies of the spine in flexion and hyperextension will reveal lesions not detected by routine methods.

EDITOR'S NOTE: This paper is discussed along with others on related subjects in Radiology **72**: 392, March 1959.

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Portland 12, Ore.

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SUMMARIO IN INTERLINGUA

Myelographia Dynamic In Position Erecte, A Grande Volumines De Substantia De Contrasto

Ingressiones in le spatio subarachnoide, emanante ab processos pathologic de origine posterior, pote esser demonstrate solmente si le superficie del canal vertebral es visualisate. Impingimentos intermittente que es causate per ponderation e motiones flexive del columna vertebral es apte a escappar completemente al observation in myelographia routinari a decubito ventral.

Un combination de myelographia in position erecte e a grande volumines de substantia de contrasto con studios del columna vertebral in flexion e hyperextension va revelar multe lesiones que non es detegite per medio de methodos routinari.

Left Atrial Calcification[1]

CHARLES W. VICKERS, M.D., OWINGS W. KINCAID, M.D., F. HENRY ELLIS, JR., M.D., and ANDRÉ J. BRUWER, M.D.

CALCIFICATION in the wall of the left atrium, appearing in association with rheumatic heart disease, was first described as a pathologic entity by Oppenheimer (1) in 1912. It was not referred to as a radiologic finding, however, until 1938, when Shanks and his co-workers (2) considered it in the differential diagnosis of intracardiac calcification. Since that time, reports of isolated cases or small series have appeared sporadically in the radiologic literature (3–14). The total number of recorded cases in which the antemortem diagnosis of calcification of the left atrial wall was established by radiologic methods is now 42. The purpose of this paper is to report 5 additional examples seen at the Mayo Clinic since 1953.

Since all the cases described, including those comprising the present study, have been associated with rheumatic heart disease of long standing, it may be assumed that left atrial calcification is pathognomonic of that condition. Although minute amounts of calcium may be present in the atrial walls in hyperparathyroidism and in certain other diseases characterized by abnormal deposition of calcium, roentgen evidence of atrial calcification has never, to our knowledge, been noted in these conditions.

The calcification may occur in the endocardium or subendocardial region, as originally described by Oppenheimer and later by other authors (6–12); or it may be within a mural thrombus (7–9). Probably the endocardial and subendocardial calcification is the end-result of severe and perhaps repeated episodes of rheumatic endocarditis (9–11), in which circumstances the calcification has occurred in necrotic or devitalized tissue. Calcification occurs in the endocardium and subendocardial region much more frequently than in thrombi. Curry and associates (7) noted that the body of the left atrium and the left auricular appendage are involved in the process with about equal frequency. Among our 5 patients, the calcification was in the endocardium in the body of the left atrium in 4 and in a thrombus in the left auricular appendage in 1.

It has been observed (8) that mitral insufficiency, with or without associated mitral stenosis, has been present in the majority of the reported cases of left atrial calcification, and from this it has been concluded that left atrial calcification in patients with rheumatic heart disease may be an indication of inoperability. Among the 5 cases with left atrial calcification which we have observed, however, mitral insufficiency was present in only 1; in the other 4 patients, all of whom underwent operation, the mitral problem was pure stenosis.

The roentgenologic manifestation of left atrial calcification is a curvilinear density up to 2 mm. in thickness in the region of the wall of the left atrium. This shell-like calcification may involve a large portion of the wall, in some instances presenting a complete ring-shaped shadow, or it may be small and sickle-shaped (9). Lamination or unusual thickness of the calcified layer is said to be suggestive of calcification of a thrombus rather than of the endocardium (7, 8). Not everyone, however, has believed that this differentiation can be made roentgenologically. Hutton (9) stated that a forked or double line of calcification is characteristic of involvement of the left auricular appendage.

In 4 of the cases comprising the present

[1] From the Mayo Clinic and Mayo Foundation (C. W. V., Fellow in Radiology; O. W. K. and A. J. B., Section of Roentgenology; F. H. E., Section of Surgery). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota. Accepted for publication in July 1958.

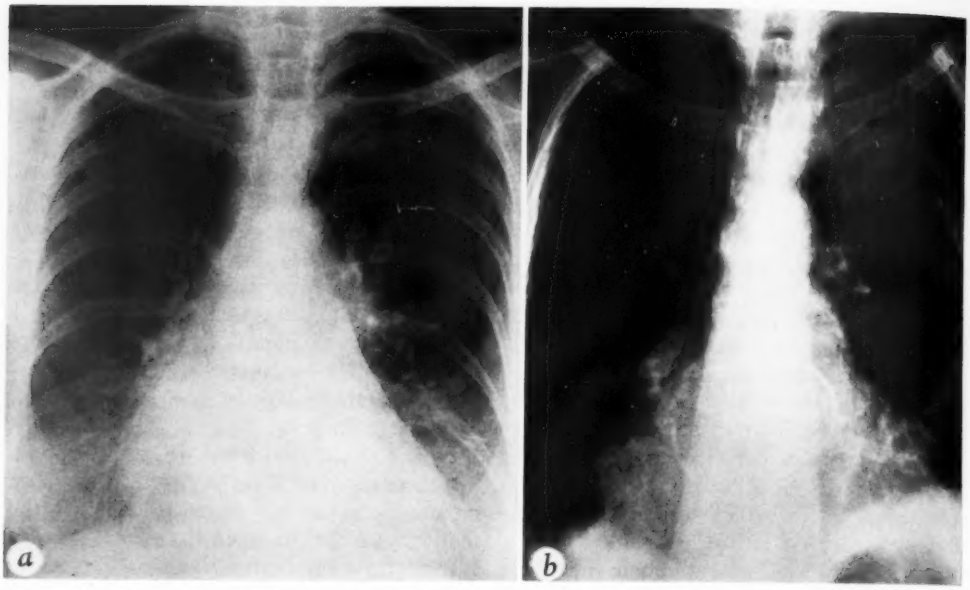

Fig. 1. Case I. *a*. Conventional postero-anterior roentgenogram of the thorax. *b*. Overpenetrated postero-anterior Bucky film showing ring-like calcification of the wall of the left atrium.

study, the calcifications were manifested as curvilinear densities involving, to various degrees, the left atrial wall. In the fifth case the calcification appeared to be forked and was found within the left auricular appendage.

Because of the density of the heart shadow and the superimposed shadow of the thoracic spine, the calcification may not be observed on the conventional roentgenogram of the thorax. It may be best demonstrated by roentgenoscopy, by roentgenograms in the right anterior oblique and lateral projections, or by overpenetrated Bucky films made in the postero-anterior projection. It may be readily demonstrated by means of tomography.

Left atrial calcification (6, 8, 13) must be differentiated from other forms of intracardiac calcification, such as that occurring in the pericardium, myocardium, coronary arteries, and cardiac valves, in primary intracardiac tumors, and in ventricular aneurysms, and also that associated with intrathoracic tumors and cysts. Calcification in other structures, such as hilar nodes and costal cartilages, which may be projected over the heart on the roentgenogram, must also be excluded. Usually the differentiation of these various conditions can be made without difficulty by means of the special examinations mentioned above.

Calcification involving a great portion of the wall of the left atrium presents a problem for the surgeon (8) in his operative approach to the mitral valve. The possibilities are: (*a*) approach by way of a pulmonary vein, (*b*) dissection through the calcified layer in the left auricular appendage, and (*c*) dissection through the calcified wall of the left atrium. All of these methods of approach increase the risk of mitral commissurotomy. The presence of left atrial calcification is, therefore, an important consideration in establishing the decision of operability from a technical standpoint.

REPORT OF CASES

CASE I: A 59-year-old woman registered at the Mayo Clinic in November 1957. The history included episodes of sore throat, edema of the ankles, and severe pain in the joints in 1906, 1918, and 1934. In 1934 she had been bedfast for three months. Since that time there had been recurrent dyspnea, orthopnea, and ankle edema, which had become progressively worse. During the past few years,

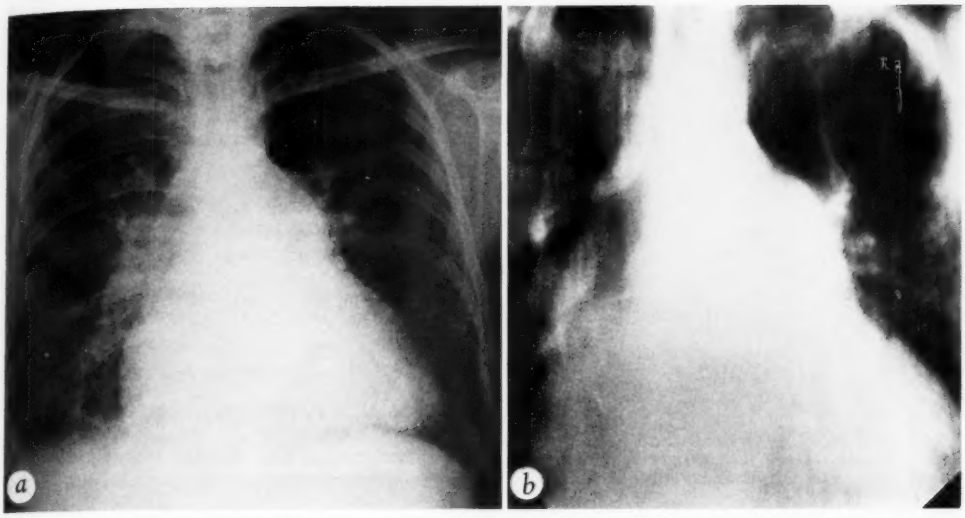

Fig. 2. Case II. *a*. Conventional postero-anterior chest roentgenogram. *b*. Tomogram of the heart showing calcification of the wall of the left atrium.

the congestive heart failure had been fairly well controlled with digitalis, diuretics, and dietary management.

Physical examination revealed a blowing diastolic murmur, grade 2 (on a basis of 1 to 4, 1 being mildest), in the mitral region. The second pulmonic sound was accentuated. The point of maximal impulse was outside the midclavicular line.

Roentgen examination of the chest revealed cardiac enlargement with mitral configuration and evidence of pulmonary vascular congestion. The left atrium was enlarged, and its wall was densely calcified, the calcification forming almost a complete ring (Fig. 1).

On Nov. 19, mitral commissurotomy was performed. At operation the entire palpable surface of the left atrium was found to be calcified. It was entered by careful dissection through a layer of calcification and thrombus in the left auricular appendage. There was no calcification in the mitral valve, and mitral insufficiency was not noted by the surgeon before or after opening the valve. The postoperative convalescence was uneventful.

CASE II: A 36-year-old woman gave no history of acute rheumatic fever. At twenty-one, during her only pregnancy, she had been partially incapacitated by dyspnea, which had been controlled by digitalis. Afterward, she had been only slightly dyspneic and had required no medication until the age of thirty-three, when she had begun to experience increased respiratory difficulty and edema of the feet and ankles. For three years, these symptoms had progressed, in spite of continuous treatment with digitalis, diuretics, and quinidine.

Physical examination disclosed the presence of auricular fibrillation. There was a systolic thrill at the base, a grade-3 systolic murmur over the aortic region, a grade-2 apical systolic murmur, and a grade-1 soft diastolic murmur at the left sternal border. Also noted were râles in the bases of both lungs, enlargement of the liver, and grade-2 pitting edema of both ankles.

A roentgenogram of the chest revealed cardiac enlargement with typical mitral configuration. In both lungs there were congestive changes, evidence of pulmonary hemosiderosis, and pleural effusion. Tomograms taken at the level of the bifurcation of the trachea showed slight elevation of the left main bronchus due to enlargement of the left atrium, and extensive calcification of the left atrial wall (Fig. 2). There was no evidence of valvular calcification on roentgenoscopy. Because of the presence of mitral insufficiency, the patient was not operated upon. After fairly satisfactory control of the cardiac decompensation was accomplished, she was dismissed.

CASE III: A 44-year-old man gave a history of acute rheumatic fever at the age of eight. No symptoms of a cardiac nature had appeared until he was thirty-eight (in 1947), when he was seen at the Mayo Clinic because of gradually progressive exertional dyspnea. Digitalis was prescribed then, but the dyspnea had become progressively more severe, and in 1948 ankle edema developed. In the years 1951 through 1953 the patient had been hospitalized on three occasions for severe episodes of congestive cardiac failure.

The preoperative physical examination in 1953 revealed a systolic thrill and a grade-1 systolic and diastolic murmur over the apex. The second pulmonic sound was accentuated, and there was electrocardiographic evidence of auricular fibrillation.

Fig 3. Case III. Overpenetrated postero-anterior roentgenogram of the thorax showing forked area of calcification in the left auricular appendage.

The cervical veins were distended and the margin of the liver was palpable two fingerbreadths below the right costal margin. There was no peripheral edema.

Roentgenography of the chest revealed cardiac enlargement with a typical mitral configuration. The pulmonary fields showed marked hemosiderosis and fluid in the right pleural space. Roentgenoscopy demonstrated enlargement of the left atrium, with a forked area of calcification in the region of the left auricular appendage on the left cardiac border (Fig. 3).

Mitral commissurotomy was performed. The surgeon noted that the left auricular appendage had been obliterated by organized thrombus and that the left atrium was enlarged. The atrium was entered through the posterolateral wall. No mitral insufficiency was noted before or after the valve was opened. The mitral orifice was exceedingly small, but the valve was not calcified.

The patient died twenty-four hours postoperatively. Necropsy established the cause of death as acute pulmonary edema. It was noted that the left auricular appendage was filled with thrombotic material which was partly calcified. There was also microscopic evidence of minute amounts of calcium in the wall of the body of the left atrium and in the wall of the left auricular appendage.

CASE IV: A 50-year-old woman gave a history of two episodes of acute rheumatic fever at eight and ten years of age. Cardiac symptoms had first been noted at the age of thirty-six (in 1943), when she began to suffer from exertional dyspnea, nocturnal dyspnea, and general malaise. In 1948 she had a cerebral embolus with associated unconsciousness, but without residual neurologic deficit. In 1950 a mitral commissurotomy had been performed, with marked improvement of symptoms. The patient had been well thereafter until early in 1957, when she had suffered a rather sudden onset of dyspnea, palpitation, and general malaise. In May 1957, cardiac catheterization revealed moderately severe pulmonary venous hypertension (pulmonary artery pressure 70 mm. Hg systolic and 44 diastolic, mean wedge pressure 35).

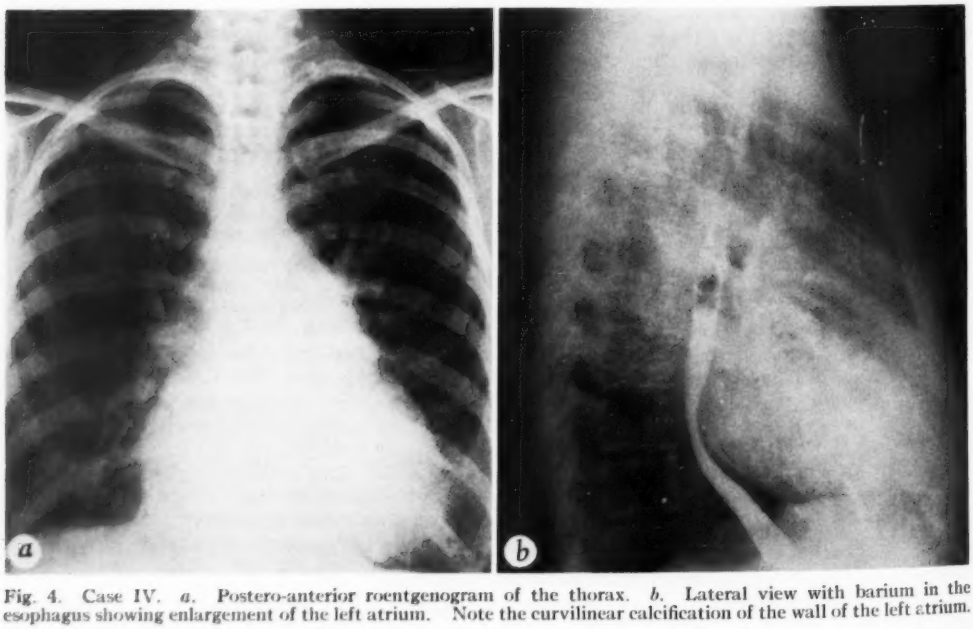

Fig. 4. Case IV. *a*. Postero-anterior roentgenogram of the thorax. *b*. Lateral view with barium in the esophagus showing enlargement of the left atrium. Note the curvilinear calcification of the wall of the left atrium.

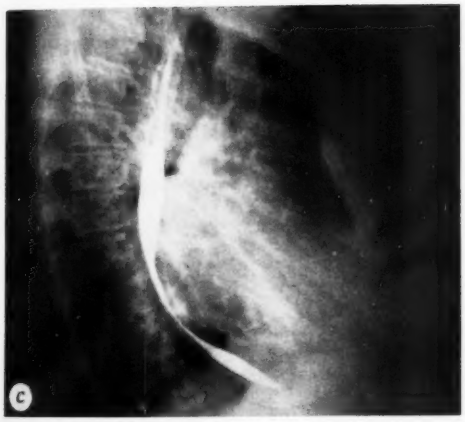

Fig. 5. Case V. *a*. Postero-anterior roentgenogram of the thorax. *b*. Overpenetrated Bucky film in left anterior oblique projection, showing left atrial calcification. *c*. Lateral view with barium in the esophagus showing enlargement of the left atrium and calcification of the wall of this chamber.

In July 1957, when first seen at the Mayo Clinic, the patient had severe exertional dyspnea and orthopnea which required her to rest in bed for sixteen to eighteen hours per day. Ankle edema had been minimal. Examination revealed moderate peripheral cyanosis. A coarse grade-2 apical diastolic murmur was present, and the second pulmonic sound was split and accentuated. The cardiac apex was in the anterior axillary line. The liver was palpable 2 cm. below the right costal margin. The electrocardiogram showed slow auricular fibrillation.

Roentgenography of the chest disclosed cardiac enlargement with typical mitral configuration. The peripheral pulmonary fields were less than normally radiolucent. Cardiac roentgenoscopy showed that the left atrium was enlarged, with ring-like calcification in its wall (Fig. 4). The mitral valve was calcified.

At a second mitral commissurotomy, Aug. 1, the surgeon noted that virtually the entire left atrial wall was solidly calcified. A small flap was dissected from this wall, and the exploring finger was forced through it at about the level of the valve. At the time the atrium was entered cardiac asystole developed, and effective circulation was maintained by cardiac massage until normal rhythm was resumed. The valve was then opened by blunt dissection and was found to be extensively calcified. The postoperative course was uneventful and the result good.

CASE V: A 57-year-old man gave no history of acute rheumatic fever or chorea. Cardiac symptoms had begun at the age of fifty (March 1950) with exertional dyspnea. Shortly after this beginning, the patient had had an arterial embolus in the left lower extremity. About one month later he had sustained a cerebral embolus with only transient signs related to the central nervous system. Since that time he had been taking bishydroxycoumarin (Dicumarol) and digitalis regularly. Exertional and nocturnal dyspnea had been progressing gradually in severity.

Examination in March 1957 revealed a grade-1 diastolic murmur over the mitral region and a grade-1 systolic murmur at the apex. The second pulmonic sound was markedly accentuated. The electrocardiogram showed right ventricular hypertrophy and auricular fibrillation.

The conventional roentgenogram of the chest revealed pronounced cardiac enlargement with typical mitral configuration. The peripheral pulmonary fields were less than normally radiolucent, and the vascular structures in the region of each hilus were prominent. Interlobular septal lines were noted in both costophrenic angles. There was fluid in the left pleural space. Cardiac roentgenoscopy indicated enlargement of the left atrium,

calcification in the wall of the left atrium, and calcification of the mitral valve (Fig. 5).

On March 18, mitral commissurotomy was performed. The surgeon noted that the left atrial wall was calcified posteriorly. No calcification was described in the left auricular appendage. The atrium was entered through the left auricular appendage and the valve was satisfactorily opened. There was no mitral insufficiency before or after the commissurotomy. The patient had a small right pulmonary embolus about ten days after operation, from which he recovered uneventfully.

COMMENT

Five cases have been presented in which calcification of the wall of the left atrium was noted roentgenologically. All five patients had severe rheumatic heart disease with involvement of the mitral valve. The mitral abnormality was pure stenosis in 4 cases, and in these mitral commissurotomy was performed. In the fifth case there was severe mitral insufficiency, and operation was not undertaken. Invariably the history of symptoms referable to the rheumatic heart disease was of long standing, the range of its duration being from seven to fifty-one years. The cardiac disability was severe in each case. In addition to calcification in the left atrial wall, the roentgen findings in each case indicated severe mitral heart disease with pulmonary venous hypertension. Mitral valvular calcification of sufficient degree to be identified roentgenologically or surgically was noted in 3 of the 5 cases. The calcification of the left atrial wall was of such magnitude or in such a position in 3 of the 4 patients operated on that the surgeon was compelled to enter the left atrium by some approach other than the usual one through the left auricular appendage. It is believed that entering the atrium through the calcified wall, through normal atrial wall near the valve, or through a pulmonary vein may be associated with a greater than average risk.

SUMMARY AND CONCLUSIONS

Calcification of the left atrial wall has been diagnosed roentgenologically in 5 cases at the Mayo Clinic since 1953. Roentgenology affords the only means for diagnosing this condition clinically. The finding is pathognomonic of severe rheumatic heart disease of long standing. It may or may not be associated with mitral insufficiency. The presence of large amounts of calcium in the wall of the left atrium presents technical problems for the surgeon which may increase the hazard of operation. Its recognition is of importance, therefore, in establishing the decision of operability.

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SUMMARIO IN INTERLINGUA

Calcification Sinistro-Atrial

Calcification del pariete del atrio sinistre esseva notate roentgenologicamente in 5 casos que omnes esseva characterisate per le presentia prolongate de rheumatic morbo cardiac con affection del valvula mitral e con hypertension pulmono-venose. In 4 patientes le anormalitate mitral esseva stenosis pur, in 1 il habeva sever grados de insufficientia. In le prime 4 casos, commissurotomia mitral esseva effectuate. In le caso con insufficientia, nulle operation esseva tentate. In 3 del 4 patientes operate, le calcification esseva de tal magnitude o in un tal position que le chirurgo se videva fortiate a entrar in le atrio sinistre per un accesso altere que le accesso usual via le appendage sinistro-auricular. Es opinate que le hasardo chirurgic es augmentate quando on entra in le atrio via le pariete calcificate, via le pariete atrial normal in le vicinitate del valvula, o via un vena pulmonar.

Roentgen Features of Nasal Accessory Sinus Mucoceles[1]

A. I. PALUBINSKAS, M.D.,[2] and HUGH DAVIES, D.M. (Oxford)

MUCOCELES of the paranasal accessory sinuses are relatively uncommon lesions which, though their etiology is still controversial and incompletely understood, are generally attributed to some form of local obstruction. Although histologically benign and slow in growth, they are prone to result in facial and ocular deformities and may on occasion produce alarming, if not ultimately serious, symptoms. Roentgenologically, they may present rather "characteristic" though not pathognomonic features. Recognition of these roentgen signs can assist the radiologist in making the correct diagnosis.

This report attempts a discussion of the clinical and roentgen features of sinus mucoceles and presents 13 cases. Included in this series are 2 instances of sphenoid sinus mucoceles. The clinical histories will be limited to the essential features, and routine blood and urine studies, where normal, will not be mentioned.

CASE I: L. H., a 45-year-old white female, was referred to Mr. Terence Cawthorne at the National Hospital for treatment of a left frontal mucocele. For three months she had suffered from left-sided frontal headaches, prominence of the left eye, and pain in the region of the left supraorbital ridge.

On examination, the patient showed a mild proptosis of the left eye. A small, tender, hard mass could be palpated just beneath the left orbital ridge in the region of the inner canthus.

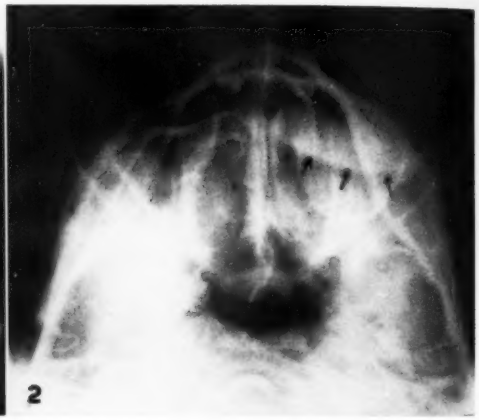

Fig. 1. Case I. Note the loss of the usual marginal scalloping of the expanded left frontal sinus.
Fig. 2. Case I. The arrows indicate encroachment of the posterior wall of the expanded left frontal sinus upon the space of the anterior cranial fossa.

Roentgenograms of the paranasal sinuses revealed destruction of the medial three-fourths of the left superior orbital rim, with slight depression of the orbital roof, bulging of the posterior wall of the frontal sinus into the space of the anterior cranial fossa, loss of the normal marginal serrations of the frontal sinus, and homogeneous increase in the density of bone adjacent to the expanded left frontal sinus. The abnormal findings were interpreted as changes secondary to a left frontal sinus mucocele (Figs. 1 and 2).

At surgery a large left frontal sinus mucocele was removed. There were bony defects in the anterior and posterior sinus walls, and the dura of the anterior fossa was exposed over a wide area.

Culture of the mucocele contents was reported as "no growth." Histologic examination of the surgical specimen showed the mucocele wall to be com-

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posed of thick fibrous tissue infiltrated with round cells, plasma cells, polymorphonuclear leukocytes, and some eosinophils. The fibrous tissue wall was covered in a few places by stratified polygonal or flattened cells and sometimes by tall columnar cells.

The patient made an uneventful postoperative recovery.

Fig. 3. Case II. The left frontal mucocele has expanded into the right frontal sinus area.

CASE II: H. C., a 58-year-old white male, was admitted to St. Bartholomew's Hospital under the care of Mr. F. C. Capps, because of progressive swelling of the left eyelid, "watering" of the left eye, and double vision, all of one year duration.

On examination the patient was found to have slight proptosis of the left eye, diplopia on right gaze, and a soft fluctuant swelling about 1 inch in diameter, outlined by a palpable bony rim, in the region of the inner supraorbital ridge.

Paranasal sinus films showed increased density of the bone adjacent to both frontal sinuses, with loss of their usual marginal serrations. The left frontal sinus was large and translucent, and there was destruction of the left superior orbital margin in its nasal half. Both antra were opaque. The findings in the left frontal sinus were interpreted as a left frontal mucocele (Fig. 3).

At surgery, this diagnosis was confirmed. Tenacious mucopus was evacuated, with immediate collapse of the swelling above the left eye. Culture of the mucocele contents was reported as showing "no growth."

The patient did well postoperatively and made an uneventful recovery.

CASE III: W. T., a 78-year-old white male, was referred to the National Hospital under the care of Mr. Wylie McKissock for investigation of proptosis. Eighteen years prior to admission a head injury had been followed by unconsciousness, and two months later the patient began to suffer from intermittent

Fig. 4. Case III. Note the degree of depression of a fragment of the right orbital roof into the space of the orbital cavity.

frontal headaches and diplopia. About nine months prior to admission the headaches became more severe and the diplopia continuous. About four weeks before admission the periorbital tissues about his right eye became swollen and tender. The patient stated that he had been deaf in the left ear since birth.

Examination revealed moderate proptosis of the right eye with deviation of the eyeball downward and outward. A tender, fluctuant swelling was palpable at the upper inner aspect of the eye with bluish discoloration of the overlying skin. Corneal reflex was less active on the right, and there was pallor of the right temporal disk.

Roentgen studies of the sinuses revealed destruction of the superior bony rim and roof of the right orbit with expansion of bony remnants of the orbital roof into the orbital cavity, slight posterior bulging of the frontal sinus into the space of the right anterior cranial fossa, and some loss of the normal marginal serrations on the lateral margins of the right frontal sinus. The lesser wing of the sphenoid on the side of the lesion showed an increase in bone density (Fig. 4).

A diagnosis of right frontal sinus mucocele was made, and at surgery a large mucocele containing dark brown fluid was removed.

Examination of the mucocele contents revealed no organisms, and culture produced no growth. Microscopic examination of the surgical specimen showed portions of cancellous bone often covered on one aspect either by cellular fibrous tissue or by dense collagenous tissue; there were also portions of fibrous tissue covered on one or both sides by ciliated columnar epithelium or stratified squamous epithelium.

The postoperative course was uneventful, and on the patient's discharge from the hospital proptosis had diminished.

Fig. 5. Case IV. Although the left superior orbital ridge has been destroyed, and there is thinning and slight depression of the orbital roof, the marginal scalloping of the left frontal sinus has not been effaced.

CASE IV: M. S., a 53-year-old white female, was admitted to the National Hospital under the care of Dr. Macdonald Critchley, with a large number of complaints, including faintness, episodes of crushing sensations in the head, prickling sensations over the head, depression, headaches, and momentary episodes of double vision.

Clinical examination revealed no abnormalities except for a 7-mm. proptosis, increased resistance to backward compression, and slight limitation of upward movement of the left eye.

Roentgenograms of the skull and sinuses showed destruction of the left superior orbital rim, with slight depression of the roof of the left orbit (Fig. 5).

A diagnosis of left frontal sinus mucocele was made and was subsequently confirmed at surgery. The mucocele was noted to have eroded the floor of the sinus.

The patient made a satisfactory postoperative recovery, and the displacement of the left eye rapidly subsided.

CASE V: A 57-year-old white male had been seen in various clinics and hospitals outside London over a period of several years complaining of swelling, pain, and impaired vision in the left eye. These symptoms allegedly followed a laceration of the left forehead sustained when his bicycle collided with a truck. X-ray examination of the skull following this accident had revealed no fracture but was reported as showing evidence of "sinusitis."

The patient had been seen by an ear, nose, and throat specialist, who noted proptosis of the left eye and obtained roentgenograms showing destruction of the superior and medial margins of the left orbit and sclerosis of the lateral bony margins of the left frontal sinus. The latter was larger and more translucent than the right frontal sinus; there was thickened mucosa in the right antrum, and the left antrum was opaque (Fig. 6).

A diagnosis of mucocele of the left frontal sinus was made and subsequently confirmed at operation. The mucocele was found to contain pus.

Postoperatively the patient failed to improve, and two weeks later a left radical antrostomy was performed, followed shortly afterward by further surgery to investigate and correct a draining abscess at the inner end of the supraorbital incision scar.

Fig. 6. Case V. Sclerosis of the lateral bony rim of the enlarged left frontal sinus. Contrast the smooth margins of the left sinus with the smudgy, irregular margins of the smaller right frontal sinus.

Two weeks after this last surgical procedure the patient experienced sudden severe pain in the right side of the chest. He was placed on intensive antibiotic therapy, but his condition steadily deteriorated, and he died two weeks later.

Postmortem, multiple pulmonary abscesses were found in association with infarcted lung tissue. The coronary arteries were grossly atherosclerotic. The pathologist attributed death to "lung abscesses following frontal and maxillary sinusitis."

CASE VI: A. W., a 55-year-old white male, was seen in the Out-patient Department of the National Hospital because of severe throbbing pain back of the left eye. Fourteen months previously he had experienced severe pain in the left cheek, eye, and forehead; roentgenograms revealed a "blocked left antrum"; operation was advised but not carried out, and the symptoms disappeared.

On clinical examination the patient had difficulty in walking straight and kept his right eye covered. There was marked but not complete ptosis on the left without evidence of proptosis or tenderness of the eye. Diplopia occurred on looking upward, downward, and to the right; the left pupil was questionably sluggish to light and reacted only through a fairly small range.

Roentgen studies of the sinuses showed thickening

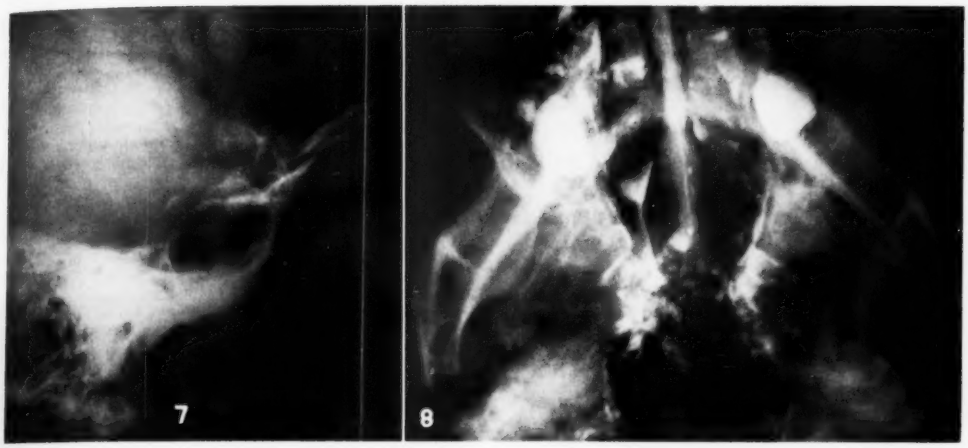

Fig. 7. Case VI. Expansion and destruction of the bony walls about the sphenoid sinus, with only a ghost shadow of the sella remaining.
Fig. 8. Case VI. Lipiodol replacement study of the sinuses. Note the expanded left sphenoidal sinus.

of the mucosa of the right antrum. The sphenoid sinuses were partially opaque, and their posterosuperior walls could not be outlined. The entire sellar region was decalcified, particularly the anterior part of the floor. Lipiodol replacement studies of the sinuses suggested a left parasellar space-occupying lesion in the region of the left sphenoidal sinus (Figs. 7 and 8).

The patient was subsequently transferred to the Atkinson Morley Hospital for further diagnostic studies and treatment. On admission there he showed a mild left ptosis without proptosis. A left common carotid arteriogram showed the carotid siphon displaced laterally and posteriorly in a smooth curve. The final radiologic impression was a left sphenoidal sinus mass expanding laterally and pressing upon the carotid siphon.

Operation was performed by Mr. R. Peacock. When the left sphenoid sinus was entered, clear, thick, glairy fluid gushed forth, apparently under considerable pressure. The mucocele had eroded the parasellar bone so that a considerable area of dura was exposed.

The patient received antibiotic therapy postoperatively and made an uncomplicated recovery.

In Table I the pertinent clinical and radiologic findings in 7 additional patients are summarized. The diagnosis of mucocele was confirmed by definitive surgery in cases VIII and XII and by biopsy and drainage in case XIII. In case VII there was a spontaneous decompression on the day prior to hospital admission, with rapid subsidence of all symptoms; Cases IX and X responded satisfactorily to conservative therapy, and Case XI was transferred without surgery to another hospital for treatment of more pressing psychiatric problems.

DISCUSSION

Definition: A definition of mucocele of the paranasal sinuses acceptable to a majority of authorities has not been made. For our purposes, however, and from a radiologic point of view, the clinical entity generally understood by the term can be described as a collection of fluid or fluid-substance enclosed in a tissue membrane within an accessory sinus or sinus compartment which, by its expansion, has thinned, expanded, deformed, and/or destroyed adjacent bony structures.

Occurrence: Although not common, the lesion is by no means rare. McNally (19) was able to find 11 cases in the records of the Royal Victoria Hospital in a period of twenty years and estimated that in a professional lifetime 5 to 10 examples might be seen by anyone directly connected with the otolaryngologic clinic of a teaching hospital. Howarth (13) reported that up to 1921 he was able to collect almost 300 cases from the literature.

Age and Sex: The sexes are about equally affected. The age span reported has been

TABLE I: CLINICAL AND ROENTGEN FEATURES OF 7 CASES

Patient Sex Age	Principal Complaint and Duration	Principal X-Ray Findings	Diagnosis and Comment
VII (G. A.) M 59	Diplopia and "dropping" of left eye, five weeks	Destruction medial left orbital rim and roof; sclerosis frontal bone; poor definition bony sinus margins	Mucocele, left frontal sinus. Spontaneous decompression one day prior to hospital admission
VIII (S. A.) M 25	Diplopia and painful proptosis of left eye, one year	Destruction medial portion left orbital rim; expansion left ethmoid sinus; sclerosis left frontal bone	Mucocele, left ethmoid sinus. Diagnosis confirmed by orbital decompression and evacuation of mucocele
IX (S. T.) F 21	Pain in left temporomandibular region, two months. Previous history of sinus operation	Expansion and homogeneous opacification of left ethmoidal air cell	Mucocele, left ethmoid sinus. Conservative therapy relieved temporomandibular pain. No operation
X (J. F.)* M 60	Headache, recurrent swelling right eye, and discharging sinus tract since sinus operation 10 years previously	Destruction medial half right superior orbital rim; sclerosis right frontal bone; opacified right antrum	Mucocele, right fontal sinus. Symptoms controlled on conservative therapy. No operation
XI (M. S.) F. middle-aged	Headaches, anxiety, indecision, and fear of going insane; duration not specified	Expansion left fronto-ethmoidal air cells into orbital cavity; some loss of marginal serrations left frontal sinus; poor definition left orbital rim (? destruction)	Mucocele, left frontal and fronto-ethmoidal sinuses. Patient severely disturbed and referred elsewhere for psychiatric treatment. No operation
XII (A. R.)† F 40	Headaches and progressive proptosis of left eye, one year	"Large extension of the left frontal sinus projecting through the image of the orbit. . .opaque and poorly pneumatized left antrum"	Mucocele, left frontal sinus. Diagnosis confirmed at operation
XIII (B. A.)† F adult	Headache, ptosis left eye, and left deafness; duration unknown	"Large growth in the posterior nasal region"	Biopsy of posterior nasal mass produced decompression of a sphenoid sinus mucocele

* Willesden General Hospital. † St. Bartholomew's Hospital.

from thirteen to eighty years (11), with the greater number of cases in adults. The onset, however, is no doubt considerably earlier than the age at which the diagnosis is made, by virtue of the indolent nature of the lesion and its slow growth. Some patients have gone as long as eighteen years after the appearance of signs or symptoms before seeking medical advice (16).

Location: The majority of mucoceles occur in the frontal and ethmoid sinuses, the frontal being most commonly involved (30). Sphenoid sinus mucoceles are rare, about 25 instances having been reported up to 1946 (16). Controversy exists regarding involvement of the maxillary sinuses (7, 8, 17, 27). Although antral mucoceles have occasionally been reported (12, 15), most authors agree that they probably do not occur (9, 23) or, if they do, are extremely rare (5, 10, 13, 27).

Wigh (31) has emphasized that some mucoceles, supposedly with their origin in the frontal sinus, actually arise in anterior ethmoidal cells and, in fact, may be in the frontal bone, lateral and separate from the frontal sinus proper. Bilateral involvement may occur, usually in the frontal sinuses, presumably from spread to both sides by extension from a unilateral focus.

Etiology: An exact definition of the etiology of these slowly expanding mucoceles is not possible. It is likely that multiple causative factors exist rather than a single one, all producing a slowly expanding collection of fluid enclosed in a membrane. Such an hypothesis would best explain the finding of mucoceles in patients both with and without antecedent sinus infection or trauma and with and without evidence of sinus ostia obstruction.

Suggested causative factors are legion.

Those cited most often include blocked sinus ostia due to infection, trauma, or congenital abnormalities; focal microscopic lesions or cystic degeneration in the mucosa; progressive distention of a mucous gland; progressive growth of "retention" cysts; degenerative changes in mucosal polyps (2, 5, 14, 18, 24, 26, 27, 30, 31).

Development of the Lesion: Notwithstanding the fact that a clear etiologic factor for paranasal mucoceles may not be evident, an examination of the natural history of their macroscopic development in the sinus cavities is helpful in assessing the clinical and roentgen findings.

As contents of the mucocele accumulate and pressure against the confining structures of the sinus or sinus compartment increases, the bony walls become thinned, expanded, and finally eroded. Since the lesion occurs almost exclusively in the frontal and ethmoid sinuses, this process most often produces clinical deformity and/or destruction of the frontal bone, superomedial orbital ridge, orbital roof, or ethmoid plates. Downward or lateral growth displaces orbital contents, with consequent proptosis, diplopia, and occasional optic nerve atrophy. Expansion with later bone erosion can occur posteriorly in the frontal bone, with consequent encroachment on the space of the anterior cranial fossa.

It is not uncommon in well developed mucoceles to find the dura exposed and pulsating brain visible through eroded bone defects (3). Armitage (1) has described a spontaneous pneumoventriculogram secondary to cranial invasion by a mucocele associated with an osteoma. O'Shea (20) has mentioned pulsating exophthalmos due to a sphenoid sinus mucocele. The rare sphenoid lesions by their expansion and consequent bone destruction can produce symptoms referable to adjacent parts of the central nervous system (20, 22).

Symptomatology: The lesion is occasionally asymptomatic, especially in its early stages, and is identified on chance x-ray examination of the skull. Generally there are no acute signs or constitutional symptoms except in those cases where the mucocele has become infected and acutely distended with pus (suppurative mucocele, pyocele).

The usual clinical picture is that of a slowly growing painless swelling in the forehead or the nasofrontal region of the orbit just above the inner canthus, with swelling and ptosis of the upper eyelid. Proptosis, usually mild to moderate, is common. Its slow development may not be apparent to the patient until brought to his attention by friends or until diplopia, blurring or diminution of vision, epiphora, or smarting of the eye occurs. Headache or pain in the region of the swelling or in the eye may be present. Episodes of unconsciousness and vision defects have been reported in patients with sphenoid sinus mucoceles, presumably from pressure in the region of the third ventricle and optic chiasm, and Simon (22) feels that sphenoid sinus mucoceles produce a definite syndrome with associated radiographic evidence sufficient for clinical diagnosis.

Infrequently the mucocele may empty its contents spontaneously, probably by bursting its envelope and spilling its contents into an unobstructed portion of the sinus, with subsequent amelioration of some or all of the patient's symptoms (*e.g.*, Case VII). Occasionally the mucocele has been found empty at operation (19). A spectacular case of such spontaneous draining of what apparently was a mucocele was reported as early as 1839 (4).

Clinical Findings: As with the symptomatology, clinical findings will vary, depending on the location of the lesion, degree and direction of expansion and thinning of bone, the rate of growth, and the presence or absence of complicating infection. Usually there is a mild to moderate degree of proptosis with outward and downward displacement of the eyeball, some limitation in eye movement, and diplopia. A clinical swelling may be evident in the frontal bone or superior naso-orbital angle. Pressure over the swelling is most often painless. Small tumors may feel bony hard, but if the expansion has been great enough to cause

sufficient thinning or erosion of the bony wall, egg-shell crepitus may be elicited or a softer compressible area outlined by a harder bony rim may be palpated.

If an ethmoid sinus is involved, intranasal examination may reveal bulging of the wall in that region.

Funduscopic examination is usually without results, but occasional reports of slight edema and vascular congestion have been made; some patients show sluggish pupillary response, optic nerve atrophy, severe proptosis, and even blindness (6, 7).

Pathology: 1. Mucocele sac: Gross examination usually reveals the mucocele wall to be thin, smooth, and atrophic. Microscopically the wall is commonly composed of a fibrous connective-tissue base showing variable degrees of round-cell infiltration. Normal ciliated columnar cells of the sinus mucosa are replaced for the most part by cuboidal cells or layers of pavement cells, with occasional groups of mucous cells. Some areas show thickened zones of fibrous connective tissue and endothelium (26).

2. Contiguous or adjacent bone: Bone margins afford evidence of changes consequent to pressure from the expanding mucocele. These reactions are evident both as rarefactive or proliferative changes. The difference in response is generally considered to be a function of the degree and rate of expansion of the mucocele. No doubt the presence of previous or active inflammation and its effects on local blood flow are also important contributing factors to the type of osteitis. Osteomata in association with mucoceles have been reported (1, 13). On occasion, however, the hyperostotic changes secondary to the mucocele are quite prominent in a discrete area (11); in such instances a mistaken diagnosis of osteoma may be made by those unfamiliar with this feature of mucoceles.

3. Mucocele contents: Notwithstanding the name, mucoceles, or at least lesions reported as such in the literature, do not always contain mucous or mucoid substance. This is one of the points of controversy in terminology previously touched upon. Some authors will not concede the diagnosis of mucocele to lesions which, although "characteristic" clinically and roentgenologically, do not prove to have mucous or mucoid contents. Reports of mucocele in the literature describe the contents as varying from light-colored serous fluid resembling cerebrospinal fluid (28) to dark, tenacious, mucoid material with or without pus (16) and thick, glairy, green fluid (13).

Roentgen Features: Several discussions of the roentgen appearances of paranasal sinus mucoceles have appeared in the English language (11, 21, 31). Early in the course, no "characteristic" findings are present. With more developed lesions, the following features, all consequent upon the natural history of the growth and development of the lesion as described, should be sought:

1. Loss of marginal scalloping of the sinus: Normally the sinus margins, particularly in the frontal sinuses, show septate or scalloped contours. Such contours are effaced by continued pressure atrophy from the mucocele, with a resultant smooth bony margin uninterrupted by indentations.

2. Presence of bony deformity and/or destruction: This may take the appearance of thinning, bulging, and expansion, or actual destruction of walls, septa, or adjacent landmarks such as the orbital rim or roof of the orbit. Posterior expansion of the frontal sinus should be looked for but may be difficult to define, if considerable bony erosion has taken place.

3. Increased size of the involved sinus: In a chronic well developed lesion, the increased size of the involved sinus as compared to the uninvolved side will be quite evident.

4. Marginal bone porosis and sclerosis: Examination of the bone at the periphery of the involved sinus will frequently reveal abnormal changes in density and sharpness of marginal outlines. No hard and fast rule can be made regarding which type of bone reaction will prevail. Although sclerosis is common, scattered areas of both resorption and hyperostosis may be evident in different regions contiguous with or adjacent to the same lesion.

5. Changes in the translucency of the sinus: Here again no dogmatic formula prevails. The degree of density of the involved sinus will be represented by a summation of the shadow densities of bone, air, and soft tissues as seen on the particular x-ray view taken. Whether the involved region appears more or less dense will depend on the amount of swelling, mucocele contents, thinned, destroyed, or thickened bone, residual clear air cells, and infection in and about the lesion.

It goes without saying that the above-outlined criteria, either singly or in combination, are not pathognomonic of a mucocele; they can be closely mimicked by any slowly growing noninvasive lesion which produces expansion and pressure atrophy of the bony sinus walls. However, their presence in combination, especially when the normal marginal scalloping has been effaced and there is a defect visible in contiguous bony structures, makes the roentgen diagnosis of mucocele likely.

Differential Diagnosis: Samuel (21) and Wigh (31) have discussed the differential diagnosis at some length. Malignant osteolytic lesions of the sinuses, by virtue of their more rapid growth rate and invasive character, tend to produce irregular areas of destruction. Osteoblastic malignant tumors also have a tendency to greater irregularity and multiplicity. Not infrequently biopsy is necessary to verify the nature of the lesion in doubtful cases, and reports have been published of instances where the clinical and roentgen findings were considered typical of mucocele but at operation were found to be due to a malignant growth (26).

Cystic dilatation of the lacrimal duct does not usually produce deformity but can cause pressure atrophy of adjacent ethmoid cells.

The outlines of osteomas are generally distinct, and the shadow more dense than reactive bone about a mucocele.

Polyps do not usually expand or distort the sinus walls.

The rarity of sphenoid mucoceles and their relatively nondistinctive appearance commonly result in a diagnosis of hypophyseal cyst or other parasellar lesion.

Other conditions to be considered in the differential diagnosis include meningiomas, vascular anomalies of the brain, inflammatory lesions of the sinus, hydatid cysts and cysts of dental origin, and cholesteatoma. Finally, an occasional normal sinus variant will cause some difficulty if too much reliance is placed on a single roentgen criterion without reference to symptomatology and clinical findings.

Treatment: Unless the lesion is producing symptoms, the mucocele may be left alone (25). Deformity or other symptoms indicate surgical intervention.

SUMMARY

The clinical and radiologic features of mucoceles of the paranasal accessory sinuses have been discussed and the roentgen criteria helpful in making the diagnosis outlined. Thirteen previously unpublished cases are included; 2 are examples of the rare sphenoid sinus mucoceles.

NOTE: The authors acknowledge their indebtedness to the Medical Committee of The National Hospital, Queen Square, and to the staff members of the various hospitals for their permission to use the hospital records and x-ray films of the cases included in this report.

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SUMMARIO IN INTERLINGUA

Aspectos Roentgenographic De Mucoceles De Sino Accessori

Le presente articulo discute le aspectos clinic e roentgenographic de mucoceles sinusal. Es presentate 13 casos, incluse 2 occurrente in le sino sphenoide. Sex casos es reportate in detalio complete. Le datos pertinente in le altere 7 es summarisate in un tabula.

Le majoritate de iste cystes occurreva in le sinos frontal e ethmoide. Le sino frontal esseva interessate le plus frequentemente. Il es probabile que un mucocel ha multiple factores causal que resulta in le crescente collection de fluido includite in un membrana. In tanto que le contento se accumula e pressa contra le confinante structuras del sino o compartimento sinusal, le parietes ossee es tenuificate, extendite, e finalmente erodite. In certe casos le lesion es asymptomatic, specialmente durante su prime stadios. Usualmente le tableau clinic es illo de un lentemente crescente tumescentia indolor in le fronte del capite o in le region nasofrontal del orbita justo supra le cantho interior, con tumescentia e ptosis del palpebra superior. Proptosis de grado moderate o leve es commun. Isto pote resultar in diplopia, obfuscation o diminution del vision, epiphora, o dolor ocular. Mal de capite o dolores in le region del tumescentia o in le oculo es etiam possibile.

Aspectos roentgenologic al quales on debe prestar attention include la perdita del normal dentellation marginal del sino, particularmente in le sino frontal; porosis e sclerosis de osso marginal; alterationes in le translucentia del sino. Iste criterios non es pathognomonic, proque illos pote esser intimemente simulate per un lentemente crescente lesion non-invasive, sed lor presentia in le un o le altere combination rende le diagnose de mucocel probabile.

A Simple and Accurate Test for Left-to-Right Cardiac Shunts[1]

K. AMPLATZ, M.D.[2] and J. F. MARVIN, Ph.D.[3]

One of the drawbacks of conventional oxygen determination as used in right heart catheterization is lack of sensitivity and accuracy. Small left-to-right shunts are missed, and in many cases the values obtained can be interpreted only in the light of the clinical findings. We have developed a new and practical test which we believe to be safe, simple, and more accurate than any other method, including conventional dye dilution.

Basic Principle: A small amount of radioactive methyl iodide is introduced into the left side of the heart by inhalation, *i.e.*, lung, pulmonary veins, left atrium, left ventricle, and aorta (1). In the presence of a left-to-right shunt, radioactive blood is sampled almost immediately after inhalation (one to three seconds) through a catheter placed in the right side of the heart. The amount of radioactivity in the blood samples is very great, because part of the highly radioactive "bolus" enters the right heart in relatively high concentration. In the absence of a shunt there is a gradual slow increase of activity commencing after seven to twelve seconds through normal venous return (Fig. 1). The activity in the venous blood is relatively low, because the radioactive methyl iodide has been diluted in many liters of blood, and part has diffused into extravascular spaces. This diffusion has been observed by other investigators using this substance for inhalation radiocardiography (2).

Localization of Shunt: A catheter is placed in the pulmonary artery, and the first inhalation is made. If early blood samples are inactive, a shunt is excluded and no further samples are necessary. If there is evidence of early appearance of activity, two additional inhalations are made with the catheter in the right ventricle and then in the right atrium, in order to localize the site of the shunt.

Method: We have developed a very simple method of producing radioactive methyl iodide which will enable any hospital to have its own "plant."[4] Ten millicuries of sodium iodide and 20 c.c. of distilled water are introduced through a rubber stopper into an empty 100-c.c. saline bottle. One drop of stable methyl iodide is added. The next day radioactive gas which has an activity of 25 microcuries per cubic centimeter can be withdrawn into stainless steel tubing for injection.

A rubber or plastic catheter is introduced into the patient's posterior nasopharynx and the head is placed under a plastic hood, which is being continuously evacuated by a suction pump. The air is drawn through an activated carbon filter which traps the exhaled and unabsorbed methyl iodide. A special stainless steel tubing in which the radioactive methyl iodide is stored is connected to the nasal catheter, and 5 to 10 microcuries are injected at the beginning of inspiration. Simultaneously, interrupted blood samples are taken through the cardiac catheter with a specially constructed sampler at a rate of one sample every two seconds (Fig. 2). The size of the samples is adjusted by changing the negative pressure within the sampler chamber. The samples are counted in a scintillation well counter, and the resulting values are plotted as a curve. From these curves the blood flow can be calculated by conventional Stewart-Hamilton technic.

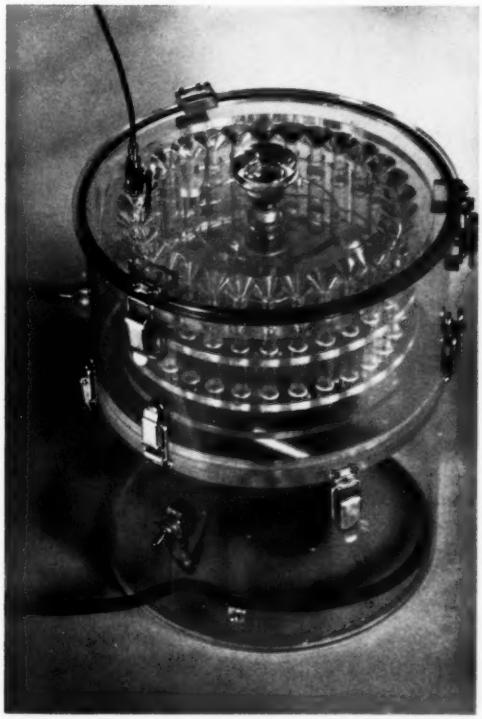

Fig. 1. Automatic sampler for interrupted blood sampling.

Metabolism: Depending upon respiration and time of injection, 90 to 99 per cent of the methyl iodide injected is absorbed. Only the first few exhalations contain small amounts of radioactivity, because after a short period of time the methyl-iodide molecule is hydrolyzed to free iodine ions. These iodine ions cannot be exhaled; consequently, the patient does not serve as a source of contamination to personnel and environment. This fact has been proved in four ways:

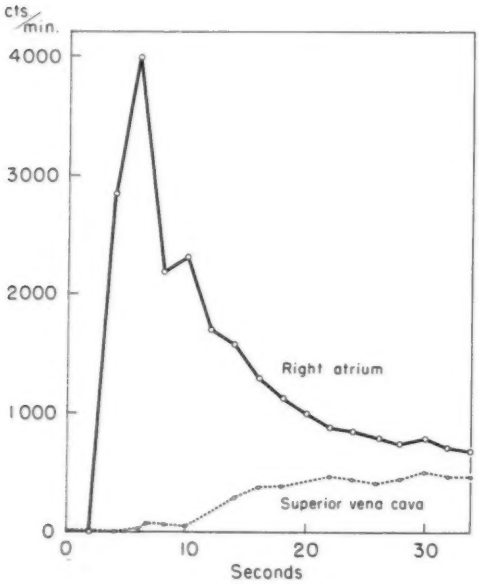

Fig. 2. Demonstration of a small interatrial septal defect. Note rapid abrupt appearance of activity in the atrium and a slow rise in the superior vena cava by normal venous return.

1. The exhaled air was collected in vacuum bottles, and no measurable activity could be detected after a few minutes.

2. Blood samples were taken and boiled for several minutes, and there was no measurable decrease in activity.

3. Normal thyroid uptake studies were obtained by inhaling radioactive methyl iodide.

4. Eighty-five to ninety-five per cent of the activity could be recovered in the urine after the thyroid had been blocked with Lugol's solution. (Biological half-life is approximately one day.)

Animals with artificially created left-to-right shunts and 14 patients with congenital heart disease have been studied by this method. Three of the patients showed evidence of a left-to-right shunt, although conventional oximetry failed to demonstrate this (surgical confirmation pending).

CONCLUSIONS

1. The method described is believed to be safe for patient and personnel.

2. It is qualitatively and quantitatively much more accurate than other accepted methods.

3. The results are obtained immediately.

4. A new field of diagnosis is opened to the radiologist.

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[1] This work was supported by a grant from The Minnesota Heart Association.

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[4] Detailed report on methods and handling in preparation.

EDITORIAL

Radiation Hazards: Fact or Fancy

Hazard is defined as "the incurring of the possibility of loss or harm for the possibility of gain" (1). Today, yesterday, and the day before, the evaluation of medicine has entered our lives. The function of the garbage man is the direct outgrowth of public-health measures. The milkman brings us milk from tuberculin-tested cows, pasteurized to kill the pathogenic bacteria. Protection of the water supply of the public is checked by repeated bacterial cultures. These measures and many others which form a background for day-to-day living are based on maximum permissible levels of service and bacterial counts. Some bacteria in milk and water are accepted, and in these instances reference to a maxium permissible level has been used. These standards were derived after many years of trial and error by an evolutionary process, whereby the permissible levels were raised or better defined. Acceptance of a maximal permissible level of irradiation, on the other hand, has been fraught with an emotional response not only by the public but by men of science.

Outbursts in the public, scientific, medical, and lay press based on emotion rather than considered judgment are excited by changes (reductions) in the maximum permissible level of irradiation. The radiologist takes the brunt of these outbursts and the word "blame" creeps in, especially when brother scientists, familiar only with the laboratory, extrapolate their findings on animals and insects to man. This is particularly true when public attention is focused on potential dangers. Extrapolations of findings in animal experiments, based on controlled complete numbers, to incomplete human eccentricities of physiology and social habits give rise to philosophic interpretation, not facts.

The good done in the production of the "potential" harm has led to many new life-saving measures and public-health technics which were not possible without an impingement on the maximal permissible level of irradiation of the world's population. The benefit to the individual and to the public derived from improved diagnostic technics necessarily enters into any consideration of radiation tolerance, but this has been de-emphasized to make the point of the argument. But, when extrapolations from the laboratory outstrip the clinical observations, the evidence must be re-examined.

Is it any wonder that the physician trained in using radiation in his practice is offended by the adjective-slinging sensationalism of the modern journalist? Already beset by threats of government controls, he becomes more defensive and unhappy under an attack which he feels is directed at his integrity. He realizes the need of better perspective on the facts. The social aspects have been confused by the entanglement of politics, where anything that implies harm to the public is a good political "pork barrel." The problem of fall-out has further confused the determination of the safe use of radiation. While it now impinges only slightly upon the maximum permissible level of radiation, it could in time interfere seriously with the medical employment of radiation essential for the benefit of the total population as well as the individual. Here again the known good must be balanced against potential harm.

Government regulation, by reasonable requirements for radiation equipment and

educational standards for "users of radiation," is being individually considered by the several states, but the problems of government regulation at a state level are many. Most important of these is the necessity of co-ordination of effort among the various disciplines within the structure of the state government. While in essence it is a matter of "public health," it also enters such fields as control of natural resources and pollution of water not even considered for human consumption directly. How does one department regulate the activities of another? Co-ordination of effort is the keynote. We physicians, who understand the effects of radiation in human tissue, must offer our services to the less informed government agencies to obtain educational and not restrictive government regulation of radiation, no matter what its source or use, if there is a possibility or desirability of human exposure either by design or accident.

The evidence on aging by radiation has been brought under question by the recent work of Kohn (2), again demonstrating the swing of the pendulum from sweeping conclusions from a single type of experimentation and observation.

The complicated problem of "radiation genetics" has been obscured by the confusion incident to injudicial extension of available material in the lower dose ranges, where the real crux of this problem lies. The Russells' most recent pronouncements (3) dwarf much of the past confusion, as premature extrapolations. The above infers a threshold or at least the concept of less sensitivity or less accumulation of genetic damage in the lower dose ranges. The accumulating "facts" are taking the "fancy" out of the interpretations of the hazards and making the discriminating scientist and physician look at the "possibility of gain" in its proper perspective. Much of the interpretation that has been applied to radiation genetics can be applied to radiation carcinogenesis in man.

The pendulum is swinging to the side of rationality as the potential good is placed higher and higher in relation to the potential harm, bringing the emphasis into the proper light of the positive rather than the negative aspects of the meaning of the word "hazard" (Lamerton, 4). This does not mean that the present day "users of radiation" (industry, medicine, and military) can relax their attempts either to reduce their doses or not add to the radiation potentials. They must meet this challenge within their own disciplines with all their ingenuity. The individual physician, particularly, must bring to bear all his sagacity to produce the best result for the individual patient with the least amount of radiation; yet keep in mind the total population effect with factual benefit weighed against potential harm. He must keep fanciful interpretations at an irreducible minimum.

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IN MEMORIAM

HARRY M. WEBER, M.D.

1899–1958

Dr. Harry M. Weber of Rochester, Minnesota, died on Oct. 4, 1958, of acute coronary-artery occlusion.

Harry Weber was born on June 30, 1899, in Lewistown, Montana. He attended St. John's University, Collegeville, Minnesota, and received the degrees of Bachelor of Science and Doctor of Medicine from the University of Minnesota in 1924 and 1926, respectively. Following his internship in St. Joseph's and Ancker Hospitals in St. Paul, he became physician in a construction camp at Berne, Washington. In January 1927, he entered the Mayo Foundation as a fellow in radiology. During the period of his training, under Drs. B. R. Kirklin, A. B. Moore, and C. G. Sutherland, he became interested in the roentgenologic diagnosis of diseases of the large intestine and in 1930 published his first paper on that subject, dealing with the double-contrast method for examining the colon.

Dr. Weber became a member of the staff of the Mayo Clinic, in the section of diagnostic roentgenology, in October 1931. Continuing his interest in the diagnosis of intestinal diseases, he soon became known as an authority in that field. Through his efforts, methods of roentgenologic diagnosis of diseases of the colon were improved and many roentgenologists began to look to him for advice concerning technics of examination and interpretation.

Shortly after joining the staff of the Mayo Clinic, he was also made a member of the faculty of the

Mayo Foundation for Medical Education and Research, a division of the Graduate School of the University of Minnesota. He was successively instructor, assistant professor, and associate professor and in 1954 became full professor of radiology. In July 1951, he was made head of the section of diagnostic roentgenology of the Mayo Clinic.

Dr. Weber contributed many articles to the radiologic literature, most of them concerned with the diagnosis of diseases of the gastrointestinal tract. He was a careful observer, an accurate analyst, and an excellent fluoroscopist. His conclusions were carefully thought out and written in precise prose. He possessed an adequate command of German and on several occasions in 1938, while visiting in Germany, he addressed meetings of radiologic societies in their native tongue.

Perhaps Harry Weber's greatest accomplishment in radiology was as a teacher. Besides being responsible for the training of graduate students in radiology at the Mayo Foundation, he was for ten years director of instructional courses of the American Roentgen Ray Society. Many radiologists learned from him the fundamentals of the roentgenologic diagnosis of intestinal disease.

Dr. Weber was certified as a specialist in roentgenology by the American Board of Radiology in 1934. He was a fellow of the American College of Radiology and a member of the Minnesota State Medical Association, the Zumbro Valley Medical Society, the Southern Minnesota Medical Association, the American Medical Association, the Minnesota Radiological Society, the American Roentgen Ray Society, the Radiological Society of North America, the Rocky Mountain Radiological Society, and the American Gastro-Enterological Association. He held honorary membership in the Detroit X-Ray and Radium Society, the St. Louis Medical Society, and the Society of Radiology and Physical Therapy of Havana, Cuba. He was a member of the Society of Sigma Xi and the fraternities of Sigma Chi and Phi Rho Sigma.

In 1940, Dr. Weber was elected president of the Minnesota Radiological Society. He served as chairman of the Section of Radiology of the American Medical Association in 1948 and was president of the American Roentgen Ray Society in 1953. In 1951, he was consultant to the committee on x-ray department planning of the American College of Radiology and in 1949 was co-chairman of the historical committee of the Minnesota State Medical Association. He served as a delegate to this latter organization for many years, representing his county medical society.

In 1937, the Fifth International Congress of Radiology awarded Dr. Weber first prize for his scientific exhibit, and in 1940 he helped prepare an exhibit on polyps of the colon and rectum which won a silver medal at the meeting of the American Medical Association. He was the recipient of several certificates of merit from the American Roentgen Ray Society. In 1948, he delivered the Russell D. Carman Memorial Lecture of the St. Louis Radiological Society, and on April 11, 1958, he delivered the first Fred Hodges Memorial Lecture at the University of Michigan.

He served as a Lieutenant Commander of the United States Navy, assigned to the Naval Hospital at Corona, California, from December 1941 to July 1942. Shortly after returning to civilian life, he suffered the first signs of the coronary heart disease which eventually was responsible for his death. Nevertheless, after recovering from the initial attack, he lived a normal, active life, showing no signs of fearing the ultimate, a fact which buoyed up several of his friends who suffered from similar conditions.

On Feb. 16, 1937, Harry Weber was married to Kathleen Osborn, who, with their three sons, Harry Osborn, Frederic William, and George Osborn, survive him.

Although interested in many sports, Dr. Weber was particularly fond of football and golf. He was an active participant in the latter sport for the last twenty years of his life and was acquainted with many of the foremost courses in the United States. He had served as president of the Rochester Golf and Country Club.

Harry took a more than average interest in the welfare of his patients, his students, and his friends. He enjoyed the company of others and delighted in hearing and telling amusing anecdotes. He was modest, kind, sincerely religious, and genuinely tolerant. The following tribute was written by one of his good friends shortly after his death, "From the flood of memories and emotions which engulf me every day as I look up from my desk to see Harry's picture, the most insistent thoughts which come to mind are those which relate to Harry's enormous capacity for steadfast friendship and his sincere and never failing modesty in evaluating his own abilities and importance. I think I have known few people more sincere in this regard."

C. ALLEN GOOD, M.D.

LESTER ALVIN SMITH, M.D.

1890–1958

With the death of Dr. Lester Alvin Smith on Dec. 15, 1958, at the age of sixty-eight, medicine lost an able physician and radiologist, his friends a wise counsellor and a good friend, and the Radiological Society of North America a dedicated and devoted member.

Dr. Smith was born in Portis, Kansas, on May 17, 1890, the son of a Methodist lay preacher. He attended Kansas Wesleyan College for three years, after which he taught in high school for one year. He then enrolled in the University of Kansas, where he earned the A.B. degree and the Master's degree in anatomy (1914) and also completed two years in medicine. This work stimulated him to seek further education at Rush Medical College in Chicago, where he received his M.D. in 1916.

Following graduation from medical school, Dr. Smith served a years internship in the Washington Boulevard Hospital, Chicago. He was appointed to a rotating internship in Cook County Hospital in 1917, but this work was interrupted for a year of service in the medical corps of the Army during World War I. At the close of the war, he returned to the Cook County Hospital staff. In 1919 he entered general practice in Aurora, Illinois. However, physical incapacity caused by an attack of hepatitis brought him back to Cook County Hospital, where, following his recovery, he stayed on as an observer in radiology. His attraction to the technic of seeking truth by examining evidence may explain the choice of radiology as his chief medical interest.

In 1921 Dr. Smith went to Indianapolis and for several years was associated in radiologic practice with Dr. A. M. Cole and Dr. R. C. Beeler. In 1922, he was radiation therapist in charge of the first deep therapy machine in the State of Indiana, at the Methodist Hospital in Indianapolis. In 1926 the major emphasis of his radiological work was in radiation therapy in the office of Drs. Beeler, Cole, Collins, and Smith. After 1932 Dr. Smith maintained his own office in Indianapolis, where he furnished radiologic consultation up to the time of his death. His many friends will not need to be reminded that he bore his last illness with courage and with a certain exasperation because it interfered with his capacity for work. He was a staff member of Methodist, St. Vincent's, Indianapolis General, and Indiana University Hospitals. He was a diplomate of the American Board of Radiology, fellow of the American College of Radiology, member of the American Radium Society, American Roentgen Ray Society, and a charter member and past president of the Indiana Roentgen Society. He belonged, also, to Nu Sigma Nu medical fraternity.

Dr. Smith was intensely interested in academic radiology and gave generously of his time to teaching in Indiana University School of Medicine, where he held the appointment of Associate Professor of Radiology. There he participated for many years in supervising radiotherapeutic procedures, tumor clinics, and postgraduate courses. During this time he provided a special fund for the establishment of a collection of teaching slides and books in the Radiology Department of the university. He was an effective instructor and he recorded his scientific observations in several publications in the radiologic literature. A testimonial dinner was given in his honor at the University in 1958, in recognition of his many years of teaching service.

During his later years, Dr. Smith voluntarily served as Chief of the Radiology Service of Indianapolis General Hospital. In this capacity, he supervised the training of a number of radiology residents and succeeded in affiliating the service as an important part of the rotating residency program of Indiana University. He was respected by his students, radiologic colleagues, and acquaintances throughout the medical profession as a fine clinician, great teacher, and true friend. His loss is deeply felt by the radiological community of Indiana.

In all his endeavors he set himself a high standard and maintained it unfalteringly. The hallmarks of his work were painstaking attention to detail combined with a precise knowledge of the latest research, and these qualities he expected of those who worked with him, were they consultants, assistants, or students.

Dr. Smith is survived by his wife, Vivian.

JOHN A. CAMPBELL, M.D.
WILLIAM M. LOEHR, M.D.

ANNOUNCEMENTS AND BOOK REVIEWS

ATLANTA RADIOLOGICAL SOCIETY

Newly elected officers of the Atlanta (Georgia) Radiological Society are: President, William C. Coles, M.D.; Vice-President, W. R. Durham, M.D.; Secretary-Treasurer, J. L. Clements, Jr., M.D., Crawford W. Long Memorial Hospital, 35 Linden Ave., N. E., Atlanta.

KANSAS RADIOLOGICAL SOCIETY

At a recent meeting of the Kansas Radiological Society, the following officers were elected: President: James R. Stark, M.D., Wichita; Vice-President, Roger K. Wallace, M.D., Manhattan; Secretary-Treasurer, Lewis G. Allen, M.D., 807 Huron Bldg., Kansas City, Kans.

NORTH FLORIDA RADIOLOGICAL SOCIETY

The North Florida Radiological Society, composed of radiologists from North Florida and South Georgia, recently elected the following officers, both from Jacksonville: M. Harlan Johnston, M.D., President; Paul A. Mori, M.D., 800 Miami Road, Secretary. Meetings are held quarterly in Jacksonville.

CANADIAN ASSOCIATION OF RADIOLOGISTS

At the twenty-second annual meeting of the Canadian Association of Radiologists held in Saskatoon, Saskatchewan, in January, the following officers were elected: President, E. M. Crawford, M.D., Montreal; Vice-President, A. E. Childe, M.D., Winnipeg; Honorary Secretary-Treasurer, Robert G. Fraser, M.D.; Associate Honorary Secretary-Treasurer, Jean-Louis Leger, M.D. The General Secretary is Miss G. A. Mollison, 1555 Summerhill Ave., Montreal 25, Que.

ASSOCIATION OF RADIOLOGISTS OF PROVINCE OF QUEBEC

Newly elected officers of the Association of Radiologists of the Province of Quebec, all of Montreal, are as follows: President, Jean Bouchard, M.D.; Vice-President, J. S. Dunbar, M.D.; Secretary, O. Raymond, M.D., 5400 Blvd. Gouin W., Montreal 9; Treasurer, L.-I. Vallée, M.D.

RADIOLOGICAL PHYSICS COURSE

A course in radiological physics, leading to the degree of Master of Science, is offered under the auspices of the Department of Radiology of the College of Physicians and Surgeons of Columbia University. It is designed to prepare candidates to carry out all the functions of a physicist in a hospital department of radiology; it would also furnish a foundation for those who wish to engage in research in radiological physics. The course includes lectures, seminars, conferences, and laboratory work. Topics included are elementary and advanced radiologic physics, electronics, radiation standardization and protection, radioactive isotopes, biostatistics, radiobiology, and clinical applications of radiation physics. Prerequisite for admission is a bachelor's degree with a major or strong minor in physics, or equivalent scholastic background, and a good academic record. A knowledge of general chemistry and general biology is desirable.

The course may be given as full-time for one year, or half-time for two years, depending on the desire of the class. The total fees amount to about $1,200.00. Further information may be obtained from Dr. Harald H. Rossi, 630 West 168th Street, New York 32, N. Y.

COURSE IN X-RAY DIAGNOSIS OF CHEST DISEASES

The Department of Radiology of Emory University School of Medicine will conduct a two-day postgraduate course in X-Ray Diagnosis of Chest Diseases, May 1–2, 1959, at the Grady Memorial Hospital in Atlanta, Ga. The guest speaker for this program will be Dr. Benjamin Felson, Professor and Director of the Department of Radiology, University of Cincinnati College of Medicine. Further information may be obtained from Dr. H. S. Weens, Postgraduate Medicine, Emory University School of Medicine, 69 Butler St., S. E., Atlanta, Ga.

COURSE IN RADIOLOGY AND PATHOLOGY OF SKELETAL SYSTEM

The Departments of Radiology and Pathology of the University of Wisconsin Medical School will present a correlated two and one-half day course on the Radiology and Pathology of the Skeletal System, May 21–23, 1959. Participating in the program will be members of the faculty of the Medical School and invited guest speakers. Among the latter will be Dr. Louis Lichtenstein, Los Angeles, Calif., Dr. H. J. Spjut, St. Louis, Mo., Dr. E. B. D. Neuhauser, Boston, Mass., and Dr. David G. Pugh, Rochester, Minn. The course, consisting of lectures, panel discussions, and round table conferences, will be held in the new Continuation Center Building of the University of Wisconsin under the direction of Drs. D. Murray Angevine and Lester W. Paul. Information concerning the

program, course fees, lodging, and other facilities may be obtained from Robert C. Parkin, M.D., Coordinator of Postgraduate Medical Education, University of Wisconsin Medical School, Madison 6, Wisc.

THYROID DISEASES SYMPOSIUM

The University of Oklahoma Medical Center will hold its Fifth Annual Surgery, Radiology, Pathology Symposium May 8–9, 1959. This year's subject will be Thyroid Diseases: Diagnosis and Treatment. The final program and further details of the meeting may be obtained from the Office of Postgraduate Education, University of Oklahoma Medical Center, 801 Northeast 13th St., Oklahoma City 4, Okla.

ATHENEUM OF RADIOLOGY, ROSARIO

The Faculty of Medicine of Rosario, Argentina, has announced the formation of an Atheneum of Radiology. Meetings will be held on the second and fourth Friday of each month in the Hospital Nacional del Centenario, Santa Fe 3100. The officers of the Atheneum are: Dr. Francisco P. Cifarelli, Chairman; Dr. Victor A. Añaños, Hospital Nacional de Centenario, Secretary; Dr. Santiago Papucci Herrera, Vice-Secretary.

GOLD MEDAL OF AMERICAN COLLEGE OF RADIOLOGY

At a meeting of the American College of Radiology in February, the Gold Medal of the College was awarded to Dr. Robert S. Stone, San Francisco, Calif., and to Dr. LeRoy Sante, St. Louis, Mo., for their many contributions to the College and to "the profession for which it stands."

ATOMIC ENERGY COMMISSION REVISION SHEET SERVICE

The United States Atomic Energy Commission has recently inaugurated a Revision Sheet service for keeping up to date the "Trilinear Chart of Nuclides" issued by the Commission in 1957. This service is available on a subscription basis from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

Letters to the Editor

To the Editor of Radiology

DEAR DOCTOR DOUB:

Dr. Leo Rigler and I have been pleased to see that our suggestions on hilar measurements made in the November 1952 issue of your journal[1] are being seriously studied by other groups. Since we noted that a large number of lesions of the hilum had been overlooked by earlier observers, we thought it would be well to devise a method of mensuration to distinguish more accurately the normal from the abnormal status in this area.

A statistical analysis of our materials gave some credence to this idea, although the end points which we used, which were accurately reported by Drs. Lodwick, Keats, and Dorst in the September 1958 issue of your journal, pages 370–374, were not sharp. These gentlemen were not quite as accurate in quoting our conclusions, however, as they were in quoting the figures which resulted from our calculations. As indicated in our paper, we were somewhat surprised at the consistency of our results but felt, nevertheless, that the clinical evaluation of experienced observers was much more reliable than this system of measurements (pages 690–691).

In Dr. Lodwick's Group I cases, in which the films of the chest were essentially negative to ordinary viewing, only 16.1 per cent would be considered well within the normal hilar measurements. In the remaining cases, presumably, a suspicion of the presence of carcinoma would have been raised by these measurements. Nowhere in our report did we state that a measurement of 11 cm. excluded the presence of carcinoma. A fairly marked overlapping was noted in our graphs, particularly in numbers 3 and 4, and from this it should be obvious that there will be many cases in which carcinoma will arise in an otherwise normal appearing hilum.

In our series it was noted that there was approximately a 16 per cent chance that the carcinomas would fall within the normal range. It is interesting to note such close correlation in these two studies. It is significant that the cases in the Lodwick series in which the lesion arose in the hilum showed a much higher percentage of abnormal measurements than did those in which the lesion was more peripherally situated.

We would like to support Doctor Lodwick's conclusion that normal hilar measurement should not mislead an observer to the assumption that a neoplasm is not present, and call attention to our final conclusion (page 692) that "critical judgment of experienced roentgenologists cannot be supplanted by these determinations, but assistance in forming the criteria for such judgment may be provided."

Thank you for this opportunity of commenting on these two papers.

Sincerely yours,
BERNARD J. O'LOUGHLIN, M.D.

[1] Radiology **59**: 683, 1952.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews

will be published in the interest of our readers and as space permits.

RADIOGRAPHIC ATLAS OF SKELETAL DEVELOPMENT OF THE HAND AND WRIST. By WILLIAM WALTER GREULICH, Professor of Anatomy, Stanford University of Medicine, and S. IDELL PYLE, Research Associate, Departments of Anatomy, Western Reserve University and Stanford University Schools of Medicine. A volume of 256 pages, with numerous figures and tables. Published by Stanford University Press, Stanford, California, 2d ed., 1959. Price $15.00.

BONE TUMORS. By LOUIS LICHTENSTEIN, M.D., Chief Pathologist, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles; Fellow, New York Academy of Medicine; Professor Extraordinario, National University of Mexico; Consultant in Bone Tumors, Tumor Tissue Registry of California Medical Association Cancer Commission; Consultant in Pathology, Los Angeles County Hospital; Consultant, City of Hope Medical Center. A volume of 402 pages, with 220 figures. Published by C. V. Mosby Company, St. Louis, Mo., 2d ed., 1959. Price $12.00.

MODERN TRENDS IN DISEASES OF THE VERTEBRAL COLUMN. Edited by REGINALD NASSIM, B.M., F.R.C.P., Physician to St. George's Hospital, Physician to the Royal National Orthopaedic Hospital, London, and H. JACKSON BURROWS, M.D., F.R.C.S., F.R.A.C.S., Orthopaedic Surgeon to St. Bartholomew's Hospital, and to the Royal National Orthopaedic Hospital; Dean, Institute of Orthopaedics, British Postgraduate Medical Federation (University of London), Consulting Orthopaedic Surgeon to the Royal Navy. A volume of 304 pages, with 172 figures. Published by Paul B. Hoeber, Inc., New York 16, 1959. Price $15.00.

ATOMIC MEDICINE. Edited by CHARLES F. BEHRENS, M.D., F.A.C.R., Rear Admiral, MC, U. S. Navy (ret.); Roentgenologist, Yater Clinic, Washington, D. C.; Consultant and Lecturer in Radiology, U. S. Naval Medical Center, Bethesda, Maryland; Formerly: Director, Atomic Defense Division, Bureau of Medicine and Surgery, Navy Department; Commanding Officer, Navy Medical Research Institute, National Naval Medical Center, Bethesda, Maryland. A volume of 706 pages, with figures and tables. Published by Williams & Wilkins Company, Baltimore, Md., 3d ed., 1959. Price $15.00.

THE PHYSIOPATHOLOGY OF CANCER BY 32 AUTHORS. Edited by FREDDY HOMBURGER, M.D. Foreword by Joseph C. Aub, M.D., Sc.D. A volume of 1,180 pages, with 189 figures and 100 tables. Published by Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York 16, N. Y., 2d ed., 1959. Price $33.00.

TRANSPLANTABLE AND TRANSMISSIBLE TUMORS OF ANIMALS. By HAROLD L. STEWART, M.D., KATHARINE C. SNELL, M.D., LUCIA J. DUNHAM, M.D., AND SAMUEL M. SCHLYEN, M.D., Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland. Atlas of Tumor Pathology, Section XII—Fascicle 40. A volume of 382 pages, with 287 figures. Published by the Armed Forces Institute of Pathology under the auspices of the Subcommittee on Oncology of the Committee on Pathology of the Division of Medical Sciences of the National Academy of Sciences—National Research Council, Washington, D. C., 1959. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C. Price $3.50.

RADIOACTIVITY MEASURING INSTRUMENTS: A GUIDE TO THEIR CONSTRUCTION AND USE. By M. C. NOKES, of the Atomic Energy Research Establishment, Harwell, England. A monograph of 76 pages, with 38 figures. Published by Philosophical Library, New York 16, N. Y., 1958. Price $4.75.

A GUIDE TO NUCLEAR ENERGY. By R. F. K. BELCHEM, C.B., C.B.E., D.S.O., American Machine & Foundry Company, formerly with T. I. Nuclear Engineering, Ltd. A monograph of 78 pages, with 13 figures. Published by Philosophical Library, New York 16, N. Y., 1958. Price $3.75.

RADIOACTIVE SULPHUR AS BENZIDINE SULPHATE: A METHODOLOGICAL STUDY WITH SPECIAL REFERENCE TO S^{35}-LABELLED PENICILLIN IN ORAL SURGERY. By ERIK ÅGREN. From the Isotope Laboratory, Department of Obstetrics and Gynecology, Sabbatsbergs Sjukhus, Karolinska Institutet, and the Department of Oral Surgery, the Royal School of Dentistry, Stockholm, Sweden. Acta Radiologica Suppl. 166. A monograph of 108 pages, with 33 figures and 23 tables. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 30:—

TIME-DOSE RELATIONSHIP AND MORPHOLOGY OF DELAYED RADIATION LESIONS OF THE BRAIN IN RABBITS. By NILS O. BERG AND MARTIN LINDGREN. Departments of Radiotherapy, Pathology, and Radiophysics, University Hospital, Lund, Sweden. Acta Radiologica Suppl. 167. A monograph of 118 pages, with 72 figures and 19 tables. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 30:—

THE RADIATION REACTION IN THE VAGINAL SMEAR AND ITS PROGNOSTIC SIGNIFICANCE: STUDIES ON RADIOLOGICALLY TREATED CASES OF CANCER OF THE UTERINE CERVIX. By OLLE KJELLGREN. From the Cytological Laboratory and the Gynecological Department of Konung Gustaf V:s Jubileumsklinik, Department of Radiotherapy, University of Gothenburg, Sweden. Acta Radiologica Suppl. 168. A monograph of 170 pages, with 27 figures, numerous charts, and 31 tables. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 35:—

LATE RESULTS OF RADIUM THERAPY IN CERVICAL CARCINOMA: A CLINICAL-STATISTICAL STUDY ON 798 PATIENTS TREATED AT THE RADIUM CENTRE, COPENHAGEN, DURING THE PERIOD 1922–1929. By BENT SØRENSEN. Acta Radiologica Suppl. 169. A monograph of 190 pages, with 44 figures and 45 tables. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 25:—

ON TOLERANCE OF BRAIN TISSUE AND SENSITIVITY OF BRAIN TUMOURS TO IRRADIATION. By MARTIN LINDGREN. Departments of Radiotherapy and Pathology, University Hospital, Lund, Sweden. Acta Radiologica Suppl. 170. A monograph of 74 pages, with 30 figures and 8 tables. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 25:—

AORTIC VALVULAR DISEASES STUDIED BY PERCUTANEOUS THORACIC AORTOGRAPHY. By PER ÖDMAN AND JAN PHILIPSON. From Roentgen Department I in collaboration with the Heart Clinic, Södersjukhuset, Stockholm, Sweden. Acta Radiologica Suppl. 172. A monograph of 60 pages, with 21 figures. Published by Acta Radiologica, Stockholm 2, Sweden, 1958. Price Sw. Kr. 25:—

L'OESOPHAGE: ACTUALITÉS HÉPATO-GASTRO-ENTÉROLOGIQUES DE L'HÔTEL-DIEU, 1957. Edited by GUY ALBOT, Médecin de L'Hôtel-Dieu and FELIX POILLEUX, Chirurgien de L'Hôpital Corentin-Celton. A volume of 274 pages, with 112 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, 6e, 1958. Price 3,600 francs.

Book Reviews

PROGRESS IN RADIATION THERAPY. Edited by FRANZ BUSCHKE, M. D., Professor of Radiology, University of California School of Medicine, San Francisco. With 13 contributors. A volume of 284 pages, with figures and tables. Published by Grune & Stratton, Inc., New York 16, 1958. Price $9.75.

In recent years, because of the increasing complexity and specialization of medicine and allied fields, a number of books have been published reporting on new developments in a particular field. In this volume Dr. Buschke has assembled a group of articles covering topics particularly related to radiation therapy which present a picture of current thought and practice. This is not an uncritical collection of reviews of recent publications, but rather a series of comprehensive but critical reviews of fundamental biological, physical, and clinical problems which have immediate application to radiation therapy. The contributors were chosen for their extensive experience in the fields under discussion.

In an extensive introduction, the editor states his objectives in the preparation of this initial volume of what is planned as a continuing series, and briefly summarizes each article. The initial contribution is a *History of Radiation Therapy* by Dr. James T. Case, and the final one a discussion of *Radiation Therapy as a Medical Specialty* by Dr. R. R. Newell. Between these limits lie discussions of fundamental biological problems of radiation action, relative biological effectiveness, time-dose relationships, and modification of radiation effects by chemical means, as well as reviews of essentially clinical problems, including ultrafractionated roentgen therapy, renal embryoma, radiation therapy of intracranial tumors and the radiation tolerance of the central nervous system, carcinoma of the thyroid, and the evaluation of radiation response in carcinoma of the cervix by cytohistologic methods. These several chapters represent clear and complete discussions of the current status in each instance. Extensive bibliographies are appended to each article.

The editor is to be congratulated on his choice of subjects and contributors. This volume is of great value to all interested in the development and advance of radiation therapy both as a review and as a source-book for more detailed study of individual topics.

CLINICAL RADIOLOGY OF ACUTE ABDOMINAL DISORDERS. By BERNARD S. EPSTEIN, M.D., Chief, Department of Radiology, The Long Island Jewish Hospital, New Hyde Park, N. Y., Associate Clinical Professor of Radiology, Albert Einstein College of Medicine, Yeshiva University, New York, N. Y. A volume of 352 pages, with 406 illustrations on 224 figures. Published by Lea & Febiger, Philadelphia, 1958. Price $15.00.

This excellent volume is a compendium of abdominal disorders. Much attention is given to acute abdominal diseases, but equal weight is accorded conditions which, though not acute, are of grave import to the patient. The disease groups are approached from an etiologic point of view. The congenital malformations and their complications are first considered, followed by the neoplastic diseases. Inflammatory disorders, parasitic and granulomatous diseases, collagen disturbances, met-

abolic conditions, and vascular disorders comprise the third major category. Traumatic disorders, foreign bodies, and effects of drugs make up a final group.

Each of the 104 individual processes considered is presented from the clinical and pathologic aspect as well as the radiologic point of view. The entire spectrum of abdominal disease is covered, from the most common to the obscure, but no attempt is made to include diseases of the urogenital tract. Attention is given primarily to the intestinal tract, and nonintestinal diseases which affect this system are approached in relation to their manifestations in the digestive organs. Emphasis is given to the excellent radiographic demonstration possible in most of the disorders described. Special views are recommended in difficult diagnostic problems where additional information is required. Illustrative radiographs are well chosen and excellently reproduced. A number of gross specimen photographs are also included.

Many of the conditions are only briefly discussed, but this is no disadvantage to the reader, since rather complete additional reading references are included for every topic.

TUMORS OF THE LUNGS AND MEDIASTINUM. By B. M. FRIED, M.D., F.C.C.P., Associate Attending Physician, Montefiore Hospital; Associate Visiting Physician, Morrisania City Hospital, New York, N. Y. A volume of 468 pages, with 340 black and white illustrations on 231 figures, and 4 in color on 2 plates. Published by Lea & Febiger, Philadelphia, 1958. Price $13.50.

While this work includes all types of pulmonary and mediastinal tumors, more than 60 per cent of the text is devoted to cancer of the lung, primary and metastatic. As would be expected in a general treatise, the material is predominantly clinical in nature, and relatively little space is devoted to radiologic aspects. Chapters on roentgen diagnosis and radiotherapy are contributed by Dr. Arnold L. Bachman and Dr. Harold W. Jacox.

After his long section on Cancer, the author has chapters on such tumors as adenoma of the bronchus, the more unusual pulmonary neoplasms, and mesotheliomas of the pleura. The last six chapters are devoted to the mediastinum, including lymphoid tumors, thymic neoplasms, teratodermoids, neurogenic tumors, and cysts.

The discussion of each tumor is preceded by a description of the anatomy and physiology of the organ of origin. Certain factors which may play an etiologic role or influence tumor growth, such as occupation and cigarette smoking, are discussed. The text is amply illustrated with photographs, some in color, roentgenograms, and line drawings.

In view of the great interest in lung cancer at the present time, this book should be of interest to the entire medical profession.

THE URETEROVESICAL JUNCTION; THE THEORY OF EXTRAVESICALIZATION OF THE INTRAVESICAL URETER. By JOHN A. HUTCH, M.D., Clinical Instructor of Urology, University of California, San Francisco. A volume of 178 pages, with 97 figures. Published by University of California Press, Berkeley 4, Calif., 1958. Price $7.50.

In this book, the work of a urologist, the physiology and anatomy of the ureterovesical junction in neurogenic and obstructive diseases is presented in detail. The first part of the text deals with the spastic neurogenic bladder and develops the author's thesis regarding the pathogenesis of upper urinary tract dilatation. Part Two deals with the ureterovesical reflux unassociated with spastic neurogenic bladder and presents the author's methods and experience in treatment of that condition.

The binding and paper are excellent. The reproductions of radiographs, of which there are many, are adequate, and the presentation concise. Urologists and radiologists particularly interested in the urinary tract should find the book of value.

SURFACE AND RADIOLOGICAL ANATOMY FOR STUDENTS AND GENERAL PRACTITIONERS. By A. B. APPLETON, W. J. HAMILTON, and IVAN C. C. TCHAPEROFF. Fourth edition by W. J. HAMILTON, M.D., D.Sc., F.R.S.E., Professor of Anatomy in the University of London at Charing Cross Hospital Medical College, sometime Regius Professor of Anatomy in the University of Glasgow, formerly Professor of Anatomy in the University of London at the Medical College of St. Bartholomew's Hospital, and G. SIMON, M.D., B.Ch., D.M.R.E. (Cantab.), F.F.R., Demonstrator of Radiological Anatomy in the Medical College of St. Bartholomew's Hospital, and Radiologist to the Diagnostic X-ray Department, St. Bartholomew's Hospital, and to the Brompton Hospital, London. A volume of 356 pages, with 416 figures. Published by The Williams & Wilkins Co., Baltimore, Md., 1958. Price $9.50.

First published in 1938, this work on *Surface and Radiological Anatomy* has now reached a fourth edition. There has been some rearrangement of the text, new illustrations have been added, and some of the original figures have been replaced. The radiological technics are now included along with general anatomy in the introductory chapter and the ensuing chapters are devoted to detailed consideration of local areas. Within this framework the arrangement is similar to that in the earlier editions.

Photographs and drawings are reproduced, together with numerous radiographs. Many photographs of surface landmarks have been retouched to show the underlying structures.

This is essentially a book on roentgen anatomy rather than a textbook of radiology. It will be found valuable for reference in any roentgen laboratory.

SYMPOSIUM ON GENETIC APPROACHES TO SOMATIC CELL VARIATION GIVEN AT RESEARCH CONFERENCE FOR BIOLOGY AND MEDICINE OF THE ATOMIC ENERGY COMMISSION. Sponsored by The Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, Held at Gatlinburg, Tennessee, April 2–5, 1958. Reprinted from Journal of Cellular and Comparative Physiology, Volume 52, Suppl. 1, December 1958. A volume of 410 pages, with figures and tables. Published by the Wistar Institute of Anatomy and Biology, Philadelphia, Penna., 1958.

From the Eleventh Biology Research Conference held at Gatlinburg, Tennessee, April 5, 1958, comes this *Symposium on Genetic Approaches to Somatic Cell Variation*. It includes some fifteen contributions, chiefly basic studies on genetics and especially, as the title indicates, somatic cell changes. The Report is available in limited quantities to qualified workers in this field from the Biology Division of the Oak Ridge National Laboratory.

HANDBUCH DER TUBERKULOSE IN FÜNF BÄNDEN. Edited by Prof. Dr. J. HEIN, Direktor des Krankenhauses Tönsheide/Holstein, Prof. Dr. h. c. H. KLEINSCHMIDT, ehemals Direktor der Kinderklinik der Universität Göttingen, Honnef, and Prof. Dr. E. UEHLINGER, Direktor des pathologischen Instituts der Universität Zürich. BAND I: ALLGEMEINE GRUNDLAGEN. Bearbeitet von H. Bloch, Pittsburgh, Pa., P. Cohrs, Hannover, K. Diehl, Bad Schwalbach, H. G. Fassbender, Mainz, E. Hedvall, Uppsala, W. Herrmann, Essen, H. Kleinschmidt, Honnef, W. Löffler, Zürich, A. Ott, Solothurn, F. Redeker, Godesberg-Mehlem, F. E. Schmengler, Bad Reichenhall, F. Schmid, Heidelberg, E. Suter, Gainesville, Florida. A volume of 832 pages, with 244 figures. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, Germany, 1958. Price DM 178—($42.40); by subscription DM 142.40—($33.80).

Upon completion, this latest German textbook on tuberculosis will exceed a total of 3,000 pages. The first volume covers the general principles; the fourth (ready for publication) will bring chapters on extrapulmonary hematogenous forms of tuberculosis; the second will present clinical aspects of pulmonary tuberculosis, the third its surgical treatment, and the final volume will be devoted to social problems (evaluation of disability, dispensaries, detection, vaccination).

This first volume consists of fourteen chapters. The "History of Tuberculosis," by W. Löffler of Zürich, is sufficiently concentrated, yet accurate, well written, and replete with chronological tables. Still, like so many medicohistorical accounts, it fails to mention anything about the age-old relationships between tuberculosis and mental illness. The "Biology of Tubercle Bacterium" and the "Experimental Immuno-Biology of Tuberculosis," by E. Suter of Gainesville, Fla., and H. Bloch of Pittsburgh, Penna., are substantial, and adequately presented. There are only thin and rather indefinite dividing lines between the chapters on "Morphology of Tuberculous Allergy" by H. G. Fassbender, "Tuberculosis and Allergy" by F. E. Schmengler, "Immunobiology" by F. Schmid, and "Tuberculin and Tuberculin Sensitivity" by H. Kleinschmidt, and consequently some overlapping was unavoidable.

There is a brief chapter on "Serodiagnosis of Tuberculosis" by W. Herrmann, reminiscent of the common "scientific" pastime of exhuming an obsolete test, giving it a fresh coat of varnish, and offering it for reconsideration. In a completely different setting, the "Epidemiology and Statistics of Tuberculosis," by F. Redeker, is an expert amplification of his 1941 report, published during wartime as *Probleme der Tuberkulosestatistik* in the ephemeral Berlin 1942 issues of *Zeitschrift der internationalen Vereinigung gegen Tuberkulose*, which is now a collector's item. Redeker's philosophy of life and his deep medical and epidemiologic convictions combine to produce a stimulating text; even those who cannot underwrite all his conclusions, will find it worthwhile to read his monograph.

The brief section on "Sources of Infection and Manner of Spread," by E. Hedvall of Uppsala, Sweden, is sufficiently integrated. In the following chapter, on "Constitutional Factors in Tuberculosis," K. Diehl shows how complicated things can become when identical twins and marker genes are involved; conversely, he simplifies matters by restating the undeniable fact that there exists an inherited (constitutional) component which plays a major role in the outcome of any individual's encounter(s) with the disease. The sections on "Tuberculosis and the Environment," and "Tuberculosis in Its Relationship to Age and Sex," by A. Ott, succeed, by way of thorough documentation, in presenting various, often contradictory points of view regarding both exogenous and endogenous factors in phthisiogenesis, usually without taking sides. The last article, by P. Cohrs, on "Comparative Pathology of Tuberculosis in Animals," is a satisfactory review, which culminates in describing the only solution thus far available for the eradication of "spontaneous" tuberculosis in susceptible animal species: sacrifice of all tuberculin-positive animals!

Reference tables are included after each chapter. There are lists of authors quoted, as well as of subjects, the latter liberally cross-indexed. The paper, the reproductions, the printing, and the binding are all excellent. The text is much easier to read than one would expect from a necessarily comprehensive presentation, handicapped also by the inherent drawbacks of plural authorship. Perhaps the only significant shortcoming is that most of these authors have given only lip service to "modern" concepts, and have otherwise endeavored to preserve their ancient be-

liefs. As of late, things in tuberculosis change so rapidly, and so frequently, that—with current delays in publication—some articles become obsolete before they are printed. Could a similar fate have befallen the first volume of this *Handbuch?*

ACTIONS CHIMIQUES ET BIOLOGIQUES DES RADIATIONS. COLLECTION DIRIGÉE PAR M. HAÏSSINSKY. TROISIÈME SÉRIE. I. RADIOLYSE DE LIQUIDES ORGANIQUES. By MILTON BURTON, Radiation Project of the Department of Chemistry, University of Notre Dame, Notre Dame, Ind. Translated from the English into French by Mme. A. Bernas. II. POLYMÉRISATIONS AMORCÉES PAR LES RADIATIONS IONISANTES. By ADOLPHE CHAPIRO AND MICHEL MAGAT, Laboratoire de chimie physique de la Faculté des sciences de Paris. III. EFFETS DES RAYONNEMENTS DE GRANDE ÉNERGIE SUR LES POLYMÈRES. By A. CHARLESBY, Royal Military College of Science, Shrivenham, Witts, England. Translated from the English into French by Mme. C Vermeil. A volume of 222 pages, with 59 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, 6°, 1958.

This is the third volume of a series on Chemical and Biological Actions of Radiations. It comprises three chapters written by outstanding men in the field of radiobiology.

The first chapter is devoted to the "Radiolysis of Organic Fluids" translated into French by Mme. A. Bernas. The author, Milton Burton of Notre Dame University, Indiana, presents a very comprehensive discussion, with all the necessary information for the radiologist interested in radiobiology. For obvious reasons his paper is condensed. Nevertheless, it includes the basic knowledge and information essential to the research worker.

Adolphe Chapiro and Michel Magat undertook the subject of "Polymerization Precipitated by Ionizing Radiations." Their work was brilliantly done in the Laboratory of Chemistry of the School of Sciences of the University of Paris. Not only the mechanism of different types of polymerizations in liquids and solids is covered, but the biological and industrial aspects as well.

From the Royal Military College of Science, England, A. Charlesby contributed "The Effect of High Energy Radiation on Polymers." The original version was translated into French by Mme. C. Vermeil. Although this work deals exclusively with high-energy radiation to long chain polymers, the author has found abundant material for an excellent monograph.

This book is a worthy addition to the two previously published volumes. The collection is a must for the library of any good radiation center.

ACTIONS CHIMIQUES ET BIOLOGIQUES DES RADIATIONS. COLLECTION DIRIGÉE PAR M. HAÏSSINSKY. QUATRIÈME SÉRIE. LES PEROXYDES ORGANIQUES EN RADIOBIOLOGIE (ORGANIC PEROXIDES IN RADIOBIOLOGY). By R. LATARJET ET AL. Colloque sur les peroxydes organiques formés par les radiations et leur rôle en radiobiologie, Institut du Radium, Paris, 9 et 10 janvier 1957. Text in original language: French or English. A volume of 156 pages, with 49 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, 6°, 1958.

This monograph—the fourth in a series on the Chemical and Biological Actions of Radiations—is a collection of papers delivered at a colloquium on organic peroxides formed by radiations and their role in radiobiology, held at the Radium Institute in Paris, Jan. 9–10, 1957. The papers are printed in the original language of each author, French or English. The monograph is also published in London by the Pergamon Press under the English title.

Some two thousand papers relating to this subject have appeared during the past few years. Dr. Latarjet organized this colloquium in an effort to summarize the important work on this phase of radiation chemistry. The contributors are outstanding workers in the field.

One is left with the feeling that much is yet to be learned about the intermediary metabolic phases of irradiation effects in cells of all kinds, but the publishing of such monographs as this help greatly to assess our stages of knowledge from time to time and thus stimulate further research.

Of interest to many radiotherapists are the papers on the influence of oxygen on the radiosensitivity of cells and tissue, modification of the oxygen effect by gases, and the mechanism of the oxygen effect.

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary*, Robert L. Brown, M.D., P. O. Box 459, Emory University, Ga.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary*, C. Allen Good, M.D., Rochester, Minn.

AMERICAN COLLEGE OF RADIOLOGY. *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

AMERICAN CLUB OF THERAPEUTIC RADIOLOGISTS. *Secretary*, Juan A. del Regato, M.D., 2200 North Cascade Ave., Colorado Springs, Colo.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS. *Secretary-Treasurer*, Paul A. Riemenschneider, M.D., 736 Irving Ave., Syracuse 10, N. Y.

SECTION ON RADIOLOGY, A. M. A. *Secretary*, T. Leucutia, M.D., 10 Peterboro, Detroit 1, Mich.

SOCIETY OF NUCLEAR MEDICINE. *Secretary*, Robert W. Lackey, M.D., 452 Metropolitan Bldg., Denver 2, Colo.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Garland Wood, Jr., M.D., Medical College of Alabama, Birmingham 3.

Arizona

ARIZONA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. Lee Foster, M.D., 1313 N. Second St., Phoenix. Annual meeting with State Medical Association; interim meeting in December.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, E. A. Mendelsohn, M.D., Holt-Krock Clinic, Fort Smith. Meets quarterly.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary*, William H. Graham, M.D., 630 E. Santa Clara St., San Jose.

EAST BAY ROENTGEN SOCIETY. *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary*, Robert B. Engle, M.D., St. Luke Hospital, Pasadena. Meets second Wednesday, September, November, March, April, and June, Los Angeles County Medical Association Building.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY. *Secretary*, Rob H. Kirkpatrick, M.D., 1219 28th St., Sacramento 16. Meets last Monday of each month, September through June.

PACIFIC ROENTGEN SOCIETY. *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually at time of California State Medical Association convention.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA. *Secretary-Treasurer*, Harold P. Tompkins, M.D., 658 S. Westlake, Los Angeles 57.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY. *Secretary*, Lee E. Titus, M.D., 164 W. Napa Street, Sonoma, Calif. Meets second Monday every other month.

SAN DIEGO RADIOLOGICAL SOCIETY. *Secretary* Stanley A. Moore, M.D., 2466 First Ave., San Diego 1. Meets first Wednesday of each month.

SAN FRANCISCO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, M. A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets quarterly, at Grison's Steak House.

SOUTH BAY RADIOLOGICAL SOCIETY. *Secretary*, Stanford B. Rossiter, M.D., 1111 University Dr., Menlo Park. Meets second Wednesday every month.

X-RAY STUDY CLUB OF SAN FRANCISCO. *Secretary*, John H. Heald, M.D., 450 Sutter St., San Francisco 8. Meets third Thursday at 7:30 P.M., Children's Hospital, September through June.

Colorado

COLORADO RADIOLOGICAL SOCIETY. *Secretary*, Lorenz R Wurtzebach, M.D., 601 E. Nineteenth Ave., Denver 5. Meets monthly, third Friday, at Denver Athletic Club.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary-Treasurer*, Ralph J. Littwin, M.D., Bristol Hospital, Bristol. Meets bimonthly, second Wednesday.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary-Treasurer*, Charles E. Bickham, Jr., M.D., 1835 Eye St., N.W., Washington 6. Meets third Wednesday, January March, May, and October, 8:00 P.M., in Medical Society Library.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Russell D. D. Hoover, M.D., 1717 N. Flagler Dr., West Palm Beach. Meets in April and October.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Joseph C. Rush, M.D., 1501 Jungle, St. Petersburg. Meets third week of October, January, April, and July.

GREATER MIAMI RADIOLOGICAL SOCIETY, *Secretary-Treasurer*, George P. Daurelle, M.D., Jackson Memorial Hospital, Miami 36. Meets monthly, third Wednesday, 8:00 P.M., at Jackson Memorial Hospital.

NORTH FLORIDA RADIOLOGICAL SOCIETY. *Secretary*, Paul A. Mori, M.D., 800 Miami Road, Jacksonville 7. Meets quarterly, March, June, September, and December.

Georgia

ATLANTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Luther Clements, Jr., M.D., 35 Linden Ave., N.E., Atlanta 8. Meets second Friday, September to May.

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Bert H. Malone, M.D., 1406 Reynolds St., Brunswick, Ga. Meets in November and at the annual meeting of the State Medical Association.

RICHMOND COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Wm. F. Hamilton, Jr., M.D., University Hospital, Augusta. Meets first Thursday of each month.

Hawaii

RADIOLOGICAL SOCIETY OF HAWAII. *Secretary-Treasurer*, Robert G. Rigler, M.D., 1020 Kapiolani St., Honolulu 14. Meets third Monday of each month.

Idaho

IDAHO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Charles R. McWilliams, M.D., Twin Falls.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary-Treasurer*, George B. Cahill, M.D., 802 Burns Ave., Flossmoor, Ill. Meets at the Sheraton Hotel, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Stephen L. Casper, M.D., Physicians and Surgeons Clinic, Quincy.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, William Meszaros, M.D., 1825 W. Harrison St., Chicago.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, Chester A. Stayton, Jr., M.D., 313 Hume Mansur Bldg., Indianapolis 4. Meets twice a year, first Sunday in May and during fall meeting of State Medical Association.

TRI-STATE RADIOLOGICAL SOCIETY (Southern Indiana, Northwestern Kentucky, Southeastern Illinois). *Secretary-Treasurer*, James R. Mathews, M.D., 118 S. E. First St., Evansville, Ind. Meets October, January, March, and May.

Iowa

IOWA RADIOLOGICAL SOCIETY. *Secretary*, James T. McMillan, M.D., 1104 Bankers Trust Bldg., Des Moines. Meets during annual session of State Medical Society, and in the Fall.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Lewis G. Allen, M.D., 807 Huron Bldg., Kansas City, Kans. Meets in the Spring with the State Medical Society and in the Winter on call.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert H. Akers, M.D., VA Hospital, Louisville 2. Meets monthly, second Friday, at Seelbach Hotel, Louisville.

Louisiana

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets second Tuesday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA. *Secretary-Treasurer*, Seymour Ochsner, M.D., Ochsner Clinic, New Orleans 15.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, W. R. Harwell, M.D., 608 Travis St. Meets monthly September to May, third Wednesday.

Maine

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Francis J. O'Connor, M.D., Augusta General Hospital, Augusta. Meets in June, October, December, and April.

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary-Treasurer*, James K. V. Willson, M.D., 1100 N. Charles St., Baltimore 1. Meets third Tuesday, September to May.

MARYLAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Nathan B. Hyman, M.D., 1805 Eutaw Place, Baltimore 17.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary-Treasurer*, Joseph O. Reed, Jr., M.D., 3825 Brush, Detroit 1. Meets first Thursday, October to May, Wayne County Medical Society rooms.

UPPER PENINSULA RADIOLOGICAL SOCIETY. *Secretary*, Arthur Gonty, M.D., Menominee. Meets quarterly.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Donald H. Peterson, M.D., 25 W. Fourth St., St. Paul 2. Meets Fall, Winter, and Spring.

Mississippi

MISSISSIPPI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Bernard T. Hickman, M.D., University of Mississippi Medical Center, Jackson. Meets monthly, on third Thursday, 6:00 P.M., at Hotel Edwards, Jackson.

Missouri

GREATER ST. LOUIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Charles J. Cherre, M.D., 462 N. Taylor, St. Louis 8. Meets on fourth Wednesday, October to May.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary-Treasurer*, Samuel B. Chapman, Jr., M.D., 830 Argyle Bldg., Kansas City, Mo. Meets last Friday of each month.

Montana

MONTANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Arthur T. Austin, M.D., 104 Doctors Bldg., Billings. Meets annually.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Warren Quinton Bradley, M.D., 206 S. 13th St., Lincoln 8. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England

CONNECTICUT VALLEY RADIOLOGIC SOCIETY. *Secretary-Treasurer*, Paul J. Kingston, M.D., 114 Woodland St., Hartford, Conn. Meets second Friday of October and April.

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, John E. Gary, M.D., 1180 Beacon St., Brookline 46, Mass. Meets third Friday, October through May, Longwood Towers, Brookline, Mass.

New Hampshire

NEW HAMPSHIRE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Paul Y. Hasserjian, M.D., 1470 Elm St., Manchester. Meets three times a year.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Andrew P. Dedick, Jr., M.D., 67 E. Front St., Red Bank. Annual meeting in May, Atlantic City; Fall meeting October or November, Newark.

New York

BROOKLYN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George A. Manfredonia, M.D., One Hanson Place, Brooklyn. Meets first Thursday of each month.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary*, Alfred H. Dobrak, M.D., 108 Pine St., Buffalo. Meets second Monday, October to May.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY. *Secretary*, Joseph A. Head, M.D., University Hospital, 150 Marshall St., Syracuse. Meets first Monday, October through May.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, C. P. Naidorf, M.D., 411 Parkside Ave., Brooklyn 26. Meets fourth Thursday, October to April (except December), at 9:00 P.M., Kings County Medical Bldg.

NASSAU RADIOLOGICAL SOCIETY. *Secretary*, Jerome Zwanger, M.D., 126 Hicksville Road, Massapequa. Meets second Tuesday, February, April, June, October, and December.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Harold G. Jacobson, M.D., Montefiore Hospital, 210th St. and Bainbridge Ave., New York 67, N. Y.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Irving Van Woert, Jr., M.D., Albany Hospital, Albany. Meets in the capital area second Wednesday, October, November, March, and April; annual meeting, May or June.

RADIOLOGICAL SOCIETY OF STATE OF NEW YORK. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets annually with the State Medical Society.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, Theodore F. VanZandt, M.D., 501 W. Main St., Rochester 8. Meets last Monday of each month, September through May.

WESTCHESTER RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Arnold Myron Wald, M.D., 406 Boston Post Road, Port Chester. Meets third Tuesday of January and October and as announced.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary-Treasurer*, Charles Bream, M.D., North Carolina Memorial Hospital, Chapel Hill, N.C. Meets in spring and fall of each year.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Marianne Wallis, M.D., Minot. Meets in the Spring with State Medical Association; in Fall or Winter on call.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary*, Francis C. Curtzwiler, M.D., 421 Michigan St., Toledo. Next annual meeting, Cincinnati, May 1959.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, William B. Schwartz, M.D., 1500 W. Third Ave., Columbus 12. Meets second Thursday, October, November, January, March, and May, 6:30 P.M., Fort Hayes Hotel, Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Frederick A. Rose, M.D., 2065 Adelbert Road, Cleveland 6. Meets at 7:00 P.M., fourth Monday, October, November, January, February, March, and April, at Tudor Arms Hotel.

GREATER CINCINNATI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John E. Singer, M.D., 19 Garfield Pl., Cincinnati 2. Meets first Monday, September through May, at Cincinnati General Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, G. F. Johnson, M.D., 1030 Reibold Bldg., Dayton 2, Ohio. Meets monthly, second Thursday, Miami Valley Hospital, Dayton

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary*, Edmond H. Kalmon, Jr., M.D., 300 Northwest 12th St., Oklahoma City.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, C. V. Allen, M.D., 9855 S.W. Hawthorne Lane, Portland. Meets monthly, second Wednesday, October to June, at 8:00 P.M., University Club, Portland.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Arch Colbrunn, M.D., 1919 Royal Oak Drive, Roseburg, Ore. Meets annually, in May.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Walter P. Bitner, M.D., 234 State St., Harrisburg. Next annual meeting, April 24–25, 1959, Harrisburg.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, Roderick L. Tondreau, M.D., 3400 Spruce St., Philadelphia 4. Meets first Thursday of each month at 5:00 P.M., from October to May, in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY. *Secretary*, Erwin Beck, M.D., 3500 Fifth Ave., Pittsburgh, 13. Meets monthly, second Wednesday, October through June, Park Schenley Restaurant.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John H. Freed, M.D., 4200 E. Ninth Ave., Denver 20, Colo. Next annual meeting, Aug. 20–22, 1959, Shirley-Savoy Hotel, Denver.

South Carolina

SOUTH CAROLINA RADIOLOGICAL SOCIETY. *Secretary*, Wayne Reeser, M.D., 1600 Ninth Ave., Conway. Meets with State Medical Association in May.

South Dakota

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA. *Secretary-Treasurer*, Donald J. Peik, M.D., 303 S. Minnesota Ave., Sioux Falls. Meets during annual meeting of State Medical Society.

The Southeast

Southern Radiological Conference. *Secretary-Treasurer*, Marshall Eskridge, M.D., 1252 Springhill Ave., Mobile, Ala.

The Southwest

SOUTHWESTERN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Gordon L. Black, M.D., 1501 Arizona Bldg., El Paso, Texas.

Tennessee

EAST TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Charles W. Reavis, M.D., Baroness Erlanger Hospital, Chattanooga. Meets in September and January, and prior to State Medical Association meeting.

MEMPHIS ROENTGEN SOCIETY. *Secretary-Treasurer*, James L. Booth, M.D., 899 Madison Ave., Memphis 3. Meets monthly first Monday, John Gaston Hospital.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James J. Range, M.D., P. O. Box 324, Johnson City. Meets annually with State Medical Association in April.

Texas

DALLAS-FORT WORTH RADIOLOGICAL CLUB. *Secretary*, Albert H. Keene, M.D., 3707 Gaston Ave., Dallas. Meets monthly, third Monday, 6:30 P.M., at the Greater Fort Worth International Airport.

HOUSTON RADIOLOGICAL SOCIETY. *Secretary*, Edward Singleton, M.D., 6621 Fannin St., Houston 25. Meets last Monday of each month at the Doctors' Club.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY. *Secretary*, Hugo F. Elmendorf, Jr., M.D., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets at Fort Sam Houston Officers' Club, third Wednesday of each month, 6:30 P.M.

TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. P. O'Bannon, M.D., 1216 Pennsylvania Ave., Fort Worth 4. Next meeting in Houston, Jan. 22–23, 1960.

Utah

UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Wm. R. Christensen, M.D., 2033 S. State St., Salt Lake City 5. Meets third Wednesday, January, March, May, September, November.

Virginia

VIRGINIA RADIOLOGICAL SOCIETY. *Secretary*, Frank A. Kearney, 2nd, M.D., 110 S. Curry St., Phoebus.

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Wayne A. Chesledon, M.D., 306 Stimson Bldg., Seattle 1. Meets fourth Monday, September through April, at College Club, Seattle.

West Virginia

WEST VIRGINIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Karl J. Myers, M.D., 112 N. Woods St., Philippi. Meets with State Medical Society, and as arranged by Program Committee.

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Joseph F. Wepfer, M.D., 5000 W. Chambers St., Milwaukee 10. Meets fourth Monday, October through May, at the University Club.

SECTION ON RADIOLOGY, STATE MEDICAL SOCIETY OF WISCONSIN. *Secretary*, Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee 2. Meets in October with State Medical Society.

WISCONSIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Farrell F. Golden, M.D., 5221 Tonyawatha Trail, Madison 4.

Puerto Rico

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA. *Secretary-Treasurer*, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, P.R.

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, Robert G. Fraser, M.D.; *Associate Honorary Secretary-Treasurer*, Jean-Louis Leger, M.D. *Central Office*, 1555 Summerhill Ave., Montreal 25, Quebec. Meets in January and June.

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALES. *General Secretary*, Louis Ivan Vallée, M.D., Hôpital Saint-Luc, 1058 rue St-Denis, Montreal 18. Meets third Saturday of each month.

L'ASSOCIATION DES RADIOLOGISTS DE LA PROVINCE DE QUEBEC. ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC. *Secretary*, O. Raymond, M.D., 5400 Blvd. Gouin W., Montreal 9. Meets four times a year.

MONTREAL RADIOLOCICAL STUDY CLUB. *Secretary*, Douglas W. MacEwan, M.D., 2300 Tupper St., Montreal 25, Quebec. Meets first Tuesday evening, October to April.

TORONTO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, L. R. Harnick, M.D., X-Ray Department, Toronto Western Hospital, 399 Bathurst St. Meets second Monday evening, September to May.

CUBA

SOCIEDAD CUBANA DE RADIOLOGÍA Y FISIOTERAPIA. *Secretary*, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Havana. Meets monthly.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA. *Headquarters*, Calle de Coahuila, Núm. 35, Mexico 7, D. F. *Secretary General*, Dr. Jorge Ceballos Labat. Meets first Monday of each month.

PANAMA

SOCIEDAD RADIOLÓGICA PANAMEÑA. *Secretary-Editor*, Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.

ABSTRACTS OF CURRENT LITERATURE

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Two New Encephalographic Signs of Pressure Hydrocephalus. M. M. Schechter, J. W. D. Bull, and P. Carey. Brit. J. Radiol. **31:** 317–325, June 1958. (National Hospital, Queen Square, London, W. C. 1, England)

Four cases of obstructing lesions of the posterior fossa are reported. Midline posterior fossa tumors were present in 2 of the cases, and aqueduct stenosis was responsible for the obstruction in the remaining 2.

Encephalography revealed markedly dilated sulci corporis callosi in all 4 cases. Four other cases—a posterior fossa meningioma and 3 acoustic neuromas—associated with large sulci corporis callosi were gleaned from the literature. Another bizarre finding in both of the authors' cases of posterior fossa tumor was the presence of an air shadow to the left of the midline and near the posterior portion of the third ventricle. This was believed to represent unilateral dilatation of the ambiens cistern, and postmortem studies with Hypaque-soaked cotton pledgets in one of the tumor cases and a normal brain confirmed this impression. Castellano and Ruggiero (Acta radiol. Suppl. 104, 1953) reproduced an encephalogram in a case of posterior fossa meningioma with an identical air shadow on the left. The authors point out that this unusual shadow should be differentiated from cavum vergae, a midline structure, and from diverticula due to rupture of the lateral ventricle in the medial angle of the trigone.

Either or both of these findings (dilated sulci corporis callosi and unilateral dilatation of the ambiens cistern) may be erronously interpreted as a manifestation of cerebral atrophy, with disastrous results. In 100 encephalograms showing cerebral atrophy, the sulci corporis callosi were filled in only 10. In 4 of these only a faint outline was obtained and in 4 others filling was "moderate." The ambiens cistern was filled in 93 of these cases but never to the degree noted in the 2 cases mentioned above.

Dilatation of the sulci and the cistern is unexpected and unexplained in these cases of obstructive hydrocephalus. One possible explanation is that some degree of atrophy may have resulted from recurrent intermittent obstruction in the early stages of tumor growth.

Nineteen roentgenograms; 2 diagrams.

SAMUEL B. HAVESON, M.D.
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A Second Variety of Hyperostosis Frontalis Interna. Annibale Casati. Radiol. med., Milan **44:** 314–316, April 1958. (In Italian) (Ambulatori Radiologici INAM, Florence, Italy)

Caput Natiforme (Babaiantz) and Hyperostosis Fronto-Parietalis (Moore). Heinz Dietrich. Radiol. clin. **27:** 249–254, July 1958. (In German) (Nervenklinik der Charité, Berlin, Germany)

Moore in 1935 (Surg., Gynec. & Obst. **61:** 345, 1935) described hyperostosis frontalis interna as a thickening of the internal table of the calvarium, while its three variants—"nebula" frontalis, hyperostosis calvariae diffusa, and hyperostosis frontoparietalis—were said to involve mainly the diploë. Casati believes that a time element is of major significance, nebula frontalis being seen in younger persons, while hyperostosis frontalis interna is supposedly a senescent condition. Moreover, he wishes to individualize a special type of this latter (senescent) hyperostosis, one characterized by a reticulated appearance.

Dietrich also goes back to Moore's classification. This he would modify so that hyperostosis frontoparietalis when it involves only the diploë is considered a developmental anomaly, while hyperostosis involving the inner table usually shows the characteristics of metabolic craniopathy. This classification of hyperostosis frontalis-parietalis is in analogy to the radiologically similar caput natiforme described by Babaiantz (Radiol. clin. **20:** 339, 1951). This latter anomaly (related to turricephaly) is frequently associated, from a roentgenologic point of view, with brachycephaly, early synostosis of the sagittal and/or coronal sutures, hypertrophy of the processus dorsi sellae, and deficient mastoid pneumatization. Associated clinical features are mental deficiency, divergent strabismus, hearing defects related to the internal ear, neurovegetative disturbances, and duodenal ulcer. In these cases the pathogenic chain starts with premature sutural closure, and for this reason they are to be considered of constitutional (developmental) origin.

Dietrich analyzed 25 cases of hyperostosis frontoparietalis and found only 4 which could be exactly fitted into Moore's classification. Eleven involved only the diploë. This group included 3 cases of typical brachycephaly, 2 in which there was shortening of the anterior cerebral fossa (presumably because of similar premature but less extensive sutural closure), and 6 with other slight developmental defects. Ten patients showed typical signs of metabolic craniopathy, and in these not only the diploë but also the internal table was involved.

Each paper is illustrated by roentgenograms.

E.R.N. GRIGG, M.D.
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Nonchromaffin Paraganglioma of the Head and Neck. Francis L. Lederer, Emanuel M. Skolnik, Burton J. Soboroff, and Elio J. Fornatto. Ann. Otol., Rhin. & Laryng. **67:** 305–331, June 1958. (1853 W. Polk St., Chicago, Ill.)

Nonchromaffin paragangliomas, called also chemodectomas, are relatively uncommon tumors arising from tissues of the carotid body at the bifurcation of the common carotid artery and in the glomus jugulare at the base of the skull, in close relation to the jugular bulb and the middle ear. The authors review the clinical, radiologic, pathologic, and therapeutic aspects of these neoplasms, reporting their own observations in 23 cases. Women are affected more often than men (five times as often in the present series). Occasionally a family history of similar lesions has been found, especially in paragangliomas of the temporal bone.

Temporal Bone Paragangliomas: Eighteen of the authors' cases involved the temporal bone. In this group the most frequent symptoms were hearing loss, otorrhea, earache, and tinnitus. In 14 cases a polypoid, richly vascular, easily bleeding mass was visible in the external auditory canal. Radiologic features include erosion and destruction of temporal bone structures adjacent to the site of the tumor. Mastoid sclerosis is an early finding. Serial roentgen studies are important both for diagnosis and for follow-up subsequent to surgery. Angiograms with opacification of the external carotid arteries may be important in differentiating nonchro-

maffin paraganglioma from acoustic neurinoma. The neurinoma does not receive the rich vascular supply characteristic of the paraganglioma.

The best treatment for the temporal bone paragangliomas is wide surgical exposure with complete radical resection. In cases where petrous bone extension is widespread and primary successful removal doubtful, palliative radiotherapy should be tried and is sometimes beneficial. Roentgen therapy and radon implantation have been used. Of 7 patients receiving both surgery and irradiation, 5 showed control of the disease after periods of four years or more, 1 was dead after two years, with intracranial extension, and 1 had no recurrence after six months. The point is made that these tumors frequently are very slow growing, with apparent temporary natural remissions, so that any relatively short-term follow-up is of doubtful significance. Complications occurred in 6 patients, including temporary or permanent nerve paralysis (facial or vagus) and serous labyrinthitis.

Paragangliomas of the Cervical Region: Symptoms of paragangliomas of the cervical region are produced chiefly by pressure against adjacent structures, most commonly the nasopharynx or adjacent cranial nerves. Radiologic findings are usually neither specific nor striking, but occasionally a bulging mass in the oro- or nasopharynx may be shown. Treatment is by surgical excision with care to avoid injury of the neurovascular structures in the neck. The dangers of therapy include hemorrhage, thrombosis of the internal carotid artery, and damage to the adjacent important nerves. Palliative irradiation may be beneficial in cases too extensive for complete removal. Roentgen therapy, cobalt therapy, and radon seeding have been described.

Four roentgenograms; 5 photomicrographs; 1 photograph; 8 tables. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Gliomas of the Optic Nerves. Henry W. Dodge, Jr., J. Grafton Love, Winchell McK. Craig, Malcolm B. Dockerty, Thomas P. Kearns, Colin B. Holman, and Alvin B. Hayles. Arch. Neurol. & Psychiat. **79:** 607–621, June 1958. (Mayo Clinic, Rochester, Minn.)

Forty-six surgically verified primary gliomas of the anterior pathways seen at the Mayo Clinic from 1915 to 1955 were analyzed. In 12 patients the tumor was confined to the optic nerve at the time of operation. The larger group of 34 patients had more diffuse gliomas involving the chiasm or optic tracts. Proptosis was the predominant finding with lesions confined to the optic nerve, while bilateral loss of vision was the outstanding symptom of the diffuse gliomas. Thirty-three of the 46 patients were children, suggesting a congenital factor.

Most of the tumors were low-grade astrocytomas, with an occasional oligodendroglioma and ganglioneuroma. All types exhibited tendencies to spread proximally. Unilateral lesions have an excellent prognosis, and cure may be expected following total removal. The diffuse tumors have a less favorable outlook.

The authors advocate a transcranial surgical approach. Enucleation of the eye or exenteration of the orbit is thought unwarranted. The role of x-ray therapy alone for tumors of the optic nerve is not evaluated.

In 8 patients with glioma confined to the optic nerve roentgenograms were obtained in the Rhese position, and in 7 of these gross enlargement of the optic foramen on the affected side was demonstrated. In only 4 of the 34 patients with involvement of the optic chiasm were roentgenograms considered to be entirely normal. The region of the chiasmatic sulcus showed a large concave depression in 8 cases and a shallower depression in an additional 8. Six patients had roentgenographic evidence of increased intracranial pressure. Pneumoencephalography on 3 patients demonstrated obliteration of the cisterna chiasmatis and lamina terminalis, posterior dislocation of the anterior portion of the third ventricle, and an outline of part of the suprasellar tumor in the cisterna interpeduncularis. Ventriculography on 4 patients showed marked obstruction of the foramen of Monroe in 3 and incomplete obstruction in 1. Only two cerebral angiograms were attempted and were considered to be normal.

Five roentgenograms; 4 photomicrographs; 6 diagrams; 1 chart; 2 tables. ROBERT S. ORMOND, M.D.
The Henry Ford Hospital

Periventricular Calcification and Cytomegalic Inclusion Disease in Newborn Infant. George Daurelle, George F. Smith, and William Riemer. J.A.M.A. **167:** 989–991, June 21, 1958. (1700 N. W. 10th Ave., Miami 36, Fla.)

A fifth case in which roentgenograms of the skull of a newborn infant showed calcium lining the walls of the lateral ventricles of the brain is reported. As in the 4 previously recorded cases, the patient displayed evidence of cytomegalic inclusion disease. In view of this association, it is suggested that the radiographic finding of periventricular calcification is indicative (and may be pathognomonic) of cytomegalic inclusion disease.

Two roentgenograms; 2 photographs.
GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

THE CHEST

Pulmonary Alveolar Proteinosis. Samuel H. Rosen Benjamin Castleman, and Averill A. Liebow with the collaboration of Frank M. Enzinger and Richard T. N. Hunt. New England J. Med. **258:** 1123–1142, June 5, 1958. (S. H. R., Armed Forces Institute of Pathology, Washington 25, D. C.)

This article originates from the Central Laboratory for Pathologic Anatomy and Research, Veterans Administration, Armed Forces Institute of Pathology, and the departments of Pathology of Harvard Medical School and Massachusetts General Hospital, and Yale University School of Medicine. It is a detailed description of the pathologic and radiographic findings in 27 cases of pulmonary disease encountered during the past five years, referred to as pulmonary alveolar proteinosis. The disease consists of filling of the alveoli by a PAS-positive proteinaceous material, rich in lipid. The material appears to be produced by the lining cells, which slough into the lumen, ultimately becoming necrotic and yielding granules and variable laminated bodies to the alveolar content. Most patients affected are adults between twenty and fifty years of age with a male predominance of 2.5:1.

The roentgenologic picture at the height of illness is similar to that of pulmonary edema. The authors describe a fine, diffuse perihilar infiltrate with a "butterfly" distribution. This infiltrate appears to radiate from the hilar structures and has a soft but slightly nodular appearance. As clinical symptoms disappear,

there is a tendency for radiographic changes to clear, but seldom is there a complete return to normal. Varying degrees of fibrotic connective tissue remain. Calcification apparently does not occur, at least for several years.

Radiographically, sarcoidosis was among the tentative diagnoses but hilar nodes were not enlarged in any of the authors' 27 cases. There is a resemblance also to *Pneumocystis* infection, but in that condition the lesions appear to be more irregularly distributed, with confluent peripheral foci that may become evident rather suddenly. In alveolar proteinosis the picture more closely simulates pulmonary edema, but this latter condition may be excluded by the duration of the changes for months or even years, during which they may clear, remain more or less stationary, or progress.

Clinically, the disease may or may not be heralded by a febrile illness. Superimposed infections may occur, in which case there is fever. Dyspnea, cough, sputum, and easy fatigability, with mild weight loss, are the most frequent features. There is no specific therapy other than antibiotics for superimposed infection.

Nothing is known of the etiology of alveolar proteinosis, although the possibility of a chemical irritant is considered. A detailed description of the gross and microscopic findings is included and 3 representative cases are reported.

Death may occur as a result of progressive filling of the alveoli or of fungal or bacterial infection. Five patients have shown definite improvement, but in only 1 case has there been concomitant resolution of the radiographic changes as evidence of apparent clinical recovery. There were 8 deaths in the series; 1 patient died as long as four years after onset of illness. The authors feel that the disease is not rare and may be increasing in incidence. They recommend that search for a causative agent by microbiologic, chemical, and epidemiologic methods be vigorously pursued.

Nine roentgenograms; 19 photomicrographs; 3 photographs; 5 tables. CAPT. NEIL E. CROW, M.C.
Lackland AFB, Texas

Farmer's Lung: An Acute Granulomatous Interstitial Pneumonitis Occurring in Agricultural Workers. Helen A. Dickie and John Rankin. J.A.M.A. **167:** 1069–1076, June 28, 1958. (J. R., 1300 University Ave., Madison 6, Wisc.)

Farmer's lung has been recognized with increasing frequency during the past several years. It is a distinct, easily recognized clinical syndrome with roentgenographic, physiological, and pathological features. Most cases occur after many years of farming and after direct exposure to moldy dust in an enclosed area with poor ventilation. The condition is to be distinguished from silo-filler's disease, which is due to irritation of the respiratory tract by the fumes created by the fermentation of nitrates in forage stored in a silo.

Clinically there is a shortness of breath during an acute febrile episode, with chills, fever, and cough. Dyspnea may be acute and frequently is associated with cyanosis. There may be a weight loss of from 10 to 20 pounds. Râles and high pitched squeaks may persist in the chest long after the chest film has returned to normal.

In 30 of the 39 cases studied, sputum examinations were done, revealing *Candida albicans* in 16. A polymorphonuclear leukocytosis with counts of 11,000 to 22,000 per cubic millimeter was found in 10 cases.

The usual roentgen finding was a diffuse interstitial pneumonitis with patchy pneumonic densities. In most cases clearing occurs in a week or two, but peribronchial accentuation may persist for a month or longer. The chest film may be normal during an acute attack. Lung biopsy reveals an acute granulomatous interstitial pneumonitis.

Two cases are reported.

Three roentgenograms; 3 photomicrographs.
GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

Extralobar (Diaphragmatic) Sequestration of the Lung. Edward J. Berman. Arch. Surg. **76:** 724–731, May 1958. (23 E. Ohio St., Indianapolis, Ind.)

In 1946 the term sequestrum was first applied to a type of pulmonary anomaly in which the blood supply of a bronchopulmonary segment is derived from the aorta rather than the pulmonary artery. This bronchopulmonary mass could be enveloped by the lung (intrapulmonary sequestration) or could exist outside an otherwise normal lung (extrapulmonary sequestration). There is no bronchial connection unless infection has caused erosion into a bronchus.

The author reports two cases, treated surgically, in which extralobar sequestration was associated with an eventration of the left hemidiaphragm. He feels that the presence of the accessory lower lobe might interfere physically with development of the diaphragm, thereby producing the eventration.

Both patients were children, three and a half and seven and a half years of age. In one the preoperative radiographic diagnosis of diaphragmatic hernia was made; in the other the preoperative radiographs suggested an eventration.

Five roentgenograms; 4 photomicrographs; 5 photographs. DEAN W. GEHEBER, M.D.
Baton Rouge, La.

Massive Pulmonary Embolism Without Infarction. Josse Kaye, G. Cohen, A. Sandler, and B. Tabatznik. Brit. J. Radiol. **31:** 326–330, June 1958. (Johannesburg Hospital, Johannesburg, Union of South Africa)

Four cases of massive pulmonary embolism are presented in detail. Autopsy was performed in 2 cases; a third patient died but autopsy was refused, and the fourth recovered.

In contrast to the findings of Westermark (Acta radiol. **19:** 357, 1938. Abst. in Radiology **32:** 634, 1939) the authors noted decreased radiolucency ("veiling") of the affected lung. Other causes of unilateral "veiling" such as poor positioning, chest wall masses, cellulitis, fluid in the main interlobar fissure, and pulmonary edema were excluded by postmortem and clinical study. In the 2 proved cases, the pulmonary artery showing an organized or adherent embolus was on the side which showed a generalized "veiling" on the radiographs. The authors stress the importance of establishing the degree of organization and adherence of an embolus to the arterial wall before deciding that a specific radiological finding resulted from the embolic event.

The pathological changes which produce the decreased radiolucency of the involved lung are unknown.

Five roentgenograms.
SAMUEL B. HAVESON, M.D.
University of California, S. F.

The Pulmonary Obstruction Syndrome in *Schistosoma mansoni* Pulmonary Endarteritis. Report of Five Cases. Ernesto J. Marchand, Raúl A. Marcial-Rojas, Roberto Rodríguez, Gerardo Polanco, and R. S. Díaz-Rivera. Arch. Int. Med. **100:** 965–980, December 1957. (E. J. M., Box 6671, Loiza St. Station, Santurce, P. R.)

The clinical, pathophysiological, and laboratory features of 5 cases of cardiopulmonary disease due to *Schistosoma mansoni* are described. Characteristically, patients with this condition are young adults from areas endemic for schistosomiasis, with no history of chronic bronchopulmonary disease. The respiratory distress which they exhibit is out of proportion to the scant pulmonary findings on physical examination. The pathological lesion in the lungs is a widespread pulmonary obliterative arteriolitis caused by repeated reinfection of the arterioles by the ova. The ensuing pulmonary artery hypertension produces right ventricular hypertrophy and eventually right-sided heart failure. Electrocardiography shows right axis deviation, right ventricular hypertrophy, and frequently an incomplete right bundle-branch block. Postero-anterior roentgenograms reveal an enlarged right ventricle which forms the left cardiac border; this is due to rotation of the heart. The aortic knob appears small or absent; the pulmonary artery segment is always dilated, sometimes aneurysmal in size. The right hilar vasculature is increased, while that on the left is inconspicuous, owing to the clockwise rotation. This radiologic picture is also seen in mitral stenosis and congenital cardiovascular defects with dilatation of the pulmonary artery. The right antero-oblique view shows absence of left atrial hypertrophy, a left ventricle of normal size, and sometimes a clear retrocardiac space. Angiocardiographic studies help to confirm the x-ray and fluoroscopic findings. The intraventricular septum is seen bulging toward the left ventricle (reverse Bernheim), secondary to the increase in right ventricular pressure. There may also be evidence on x-ray examination of pulmonary schistosomiasis, characterized by fine mottling of diffuse character. Sometimes nodular infiltrations may be present, as in one of the authors' cases. The most important pulmonary finding is, however, the rather pleoanemic middle and peripheral lung fields.

The differentiation of schistosomal cor pulmonale from that due to pulmonary parenchymal disease and primary heart disease with failure is of paramount importance. Further observation will disclose more about the natural course and prognosis of this disease. At present the outlook is poor once cardiac decompensation supervenes. Only 1 of the authors' patients was alive at the time of the report.

Five similar cases of schistosomal cor pulmonale are mentioned in an addendum.

Fourteen illustrations, including 4 roentgenograms; 1 table.

Granulomata of the Mediastinum Surgically Treated and Followed Up to Nine Years. Karl E. Karlson and Joseph J. Timmes. J. Thoracic Surg. **35:** 617–627, May 1958. (K. E. K., U. S. Naval Hospital, St. Albans, N. Y.)

This report is concerned with 19 patients who were subjected to exploratory thoracotomy for mediastinal tumors which proved to be granulomas. In most instances a mediastinal mass was discovered on routine roentgen examination. Two patients had some discomfort in the chest and 1 had pain in the right shoulder and right arm. Two patients had a slight daily elevation of temperature for three weeks prior to admission. Four patients gave a history of cough, 1 with hemoptysis, several years previously. In 1 patient who complained of fever, malaise, and weight loss, overt pulmonary tuberculosis developed two months postoperatively. Physical examination was noncontributory in each case.

Fifteen of these granulomas presented roentgenologically as masses projecting from the mediastinum to the right, above the hilus of the right lung. Typically, they were situated in the right paratracheal region, were usually lobulated, and occasionally showed spotty calcification. Tomography was useful in delineating their size, position, and character. One mass was located beneath the carina of the trachea, 1 at the left hilus, and 1 at the left heart border. In 1 patient encroachment of the mass upon the esophagus suggested the possibility of an esophageal leiomyoma. The tumors ranged in size from 2.5 to 8 cm. in the largest dimension. In no instance was there either significant hilar adenopathy or a lesion in the lung fields. In none of the cases was there any concomitant lesion visible roentgenographically or evidence on physical examination which made it possible to conclude that the mediastinal mass was definitely tuberculous or fungous in origin and not a mediastinal tumor of other type.

All of the tumors were found to be granulomata histologically. Some were described by the pathologist as "fibrocaseous granulomata" and others simply as "granulomata." All of the lesions were examined microscopically for acid-fast bacilli and 18 were cultured for *Mycobacterium tuberculosis*. Three were positive for *Mycobacterium tuberculosis* on culture. One which was negative on culture was positive for acid-fast bacilli microscopically. One granuloma was positive for *Histoplasma capsulatum*.

All of the patients recovered from thoracotomy without complication. All have been followed up to nine years, and with 2 exceptions have been asymptomatic, without evidence of further disease. In 1 patient, as mentioned above, pulmonary tuberculosis developed two months postoperatively; treatment with streptomycin and para-aminosalicylic acid was instituted and continued for eight months. At the time of writing, the patient was symptom-free. In the other case, cavitary pulmonary tuberculosis was found in the right upper lobe four years postoperatively and the patient is still under treatment.

A definite diagnosis of mediastinal granuloma cannot be made without biopsy. Excision of as much of the mass as is feasible without undue risk is accompanied by no further complications than biopsy alone. The authors believe that unless a nontuberculous etiology is established, postoperative antituberculous therapy should be administered routinely for six to twelve months.

Two roentgenograms; 1 table.

Widened Roentgenographic Mediastinal Shadow (Thymus?) and Allergy in Childhood. Jerome Glaser, Joseph L. Aponte, and Percy Barsky. J. Pediat. **52:** 267–269, March 1958. (J. G., 300 S. Goodman St., Rochester 7, N. Y.)

The authors reviewed the records of 614 children who had been treated by roentgen rays from two to twenty-seven years prior to 1953 for what was diagnosed roent-

genographically as thymic enlargement. The material was gathered in the course of the investigation by Simpson *et al.* of the incidence of neoplasia in children treated with x-rays in infancy for thymic hyperplasia (Radiology **64:** 840, 1955). The cases were taken serially from files made available by radiologists and pediatricians of Rochester, N. Y. The controls consisted of untreated siblings, and the group as a whole may be considered representative of the heterogeneous population of a northern metropolitan American city.

It was found that 173 of the 614 children (28.2 per cent) later suffered from bronchial asthma, hay fever, or eczema. These allergic conditions developed in only 106 of the 1,287 controls (8.2 per cent). While in most instances there were no roentgenograms in the sibling series, the authors believe that it is fair to state that allergic disease is significantly more frequent in children whose chest roentgenograms show broad mediastinal shadows, with or without respiratory symptoms, which were formerly attributed to an enlarged thymus gland, than in children with normal roentgenograms or with no such symptoms. This brings up the possibility that symptoms formerly ascribed to the presence of thymic hypertrophy may in fact, in many instances, have been those of allergic disease. The so-called enlargement of the thymus may also, in the allergic or potentially allergic child, be merely a part of the general lymphoid hyperplasia that characteristically occurs in many allergic children.

One table.

THE HEART AND BLOOD VESSELS

Radiologic Aspects of Operable Heart Disease. VI. Changes Following Surgical Closure of Patent Ductus Arteriosus. Philip Strauss, Herbert L. Abrams, and Saul Robinson. Circulation **17:** 1047–1055, June 1958. (Stanford University School of Medicine, San Francisco 15, Calif.)

Seventy-one cases of surgically closed patent ductus with adequate pre- and postoperative studies were analyzed to determine the magnitude, character, and timing of postoperative changes visible radiologically. Preoperatively the left atrium, both ventricles, and the pulmonary arteries were usually enlarged. In patients above the age of ten the aortic knob was frequently prominent. Postoperatively the heart and pulmonary vessels began to show a decrease in size within a few days (the pulmonary vessels seemed smaller in a few hours). By the end of two months these changes were well advanced, and after six months practically no further shrinking could be detected.

The authors mention two groups of cases in which there was a failure of the expected diminution size: those with complicating valvular lesions (most often aortic) and those with irreversible pulmonary hypertension and partial or complete reversal of the left-to-right shunt. In the latter group progressive right heart failure occurs, since the ductus acts as a safety valve.

[A third group which does not respond to surgery consists of those in whom the cardiac hypertrophy and dilatation have developed to the point of irreversibility before surgery.]

Ten roentgenograms; 2 tables.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Nonpenetrating Traumatic Injury of the Aorta. Loren F. Parmley, Thomas W. Mattingly, William C. Manion, and Edward J. Jahnke, Jr. Circulation **17:** 1086–1101, June 1958. (Walter Reed Army Hospital, Washington, D. C.)

The authors analyzed 296 cases of nonpenetrating aortic lacerations from the Armed Forces Institute of Pathology. Surprisingly about one-fifth of the patients survive at least for a time, and a few indefinitely, even with extensive laceration. In these cases a false aneurysm forms, which prevents the hemorrhage from becoming fatal. The threat of eventual rutpure, however, is always present. Diagnosis is important, since the most common site of injury is at the isthmus, an area susceptible to surgical attack.

X-ray evidence of these injuries consists of mediastinal widening and hemothorax. According to the authors' addendum, retrograde aortography best delineates the lesion, but no illustration is given.

Eight roentgenograms; 6 photomicrographs; 8 photographs; 3 tables. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Anomalous Origin of the Left Coronary Artery: The Physiologic Defect and Suggested Surgical Treatment. Robert B. Case, Andrew G. Morrow, Wendell Stainsby, and John O. Nestor. Circulation **17:** 1062–1068, June 1958. (National Heart Institute, Bethesda, Md.)

Anomalous origin of the left coronary artery from the pulmonary artery has a very grave prognosis. Most patients with this anomaly die in infancy.

Two cases are presented, in one of which an attempt was made to create an artificial supravalvular stenosis in the pulmonary artery in hope of increasing pulmonary artery pressure and thereby improving circulation in the anomalous coronary. The patient, aged nine months, died during the operation. Postmortem perfusion studies showed extensive anastomoses between right and left coronaries with retrograde flow into the pulmonary artery immediately. In the second case the anomalous left coronary origin was diagnosed clinically and electrocardiographically. Coronary arteriography resulted in filling of the right coronary initially, while the left filled within three seconds from anastomotic channels. Flow of the opaque medium into the pulmonary artery could not be detected, probably because of dilution. Selective angiocardiography with injection directly into the right ventricle failed to show the aberrant vessel. Typical thinning and dilatation of the left ventricle was noted, confirming the clinical diagnosis. Surgery was refused.

The authors believe that the flow in the anomalous coronary is actually into the pulmonary artery in most instances, and that the insufficiency of the left ventricle is caused by the blood following the path of least resistance instead of entering the myocardium. The surgical procedure of choice, therefore, seems to be ligation of the left coronary artery at its origin (physiological termination) from the pulmonary artery. Three cases are reported in which this operation was tried. In one case the patient died ten hours postoperatively; the second improved but died two months after surgery; the third was living at the time of writing, after a short interval [exact period not stated].

Three roentgenograms; 2 electrocardiograms.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Coronary Insufficiency Associated with Oral Administration of Gall-Bladder Dye. David Littmann and Frank I. Marcus. New England J. Med. **258:** 1248–1250, June 19, 1958. (VA Hospital, West Roxbury, Mass.)

Four cases of fatal coronary artery disease, with cardiovascular collapse or symptoms of coronary occlusion occurring from a few minutes to a few hours after ingestion of iodoalphionic acid (available as "Priodax") or iodopanoic acid (available as "Telepaque") are reported. The patients, males from thirty-eight to seventy years of age, all had a past history of myocardial infarct or angina pectoris. All had had chest pain within three weeks of the gallbladder examination. The possibility that the connection between the examination and the fatal coronary accidents was purely fortuitous is not ruled out. If there is a causal relation, the authors suggest that it may involve gastrointestinal irritation with increased vagal tone. They recommend premedication with atropine to suppress vagal activity if cholecystography must be done in patients with recent symptoms of coronary artery disease.

GARTH R. DREWRY, M.D.
Oakland, Calif.

Anomalous Drainage of Pulmonary Veins Detected on "Plain" Roentgenograms. Michele Sossai. Radiol. med., Milan **44:** 327–337, April 1958. (In Italian) (Istituto di Radiologia dell'Università di Padova, Italy)

The pulmonary veins, instead of draining "normally" into the left atrium, can terminate anomalously in (1) the superior vena cava, (2) the inferior vena cava, (3) the persistent left-sided vena cava, (4) the right atrium, (5) the innominate vein, (6) the azygos, (7) the subclavian, (8) the venous sinus, (9) the portal vein, or even (10) the ductus arteriosus. These deviations may be partial or total and are often associated with other congenital cardiovascular malformations. Retrospective evaluation, after cardiac catheterization, angiocardiography, and/or surgical exploration in proved cases, revealed that these venous anomalies could be detected, or at least suspected, on the basis of routine roentgenography, especially when corroborated by tomographic and kymographic findings.

Signs *common to all* these various pulmonary venous abnormalities are localized or generalized hypervascularization of the pulmonary bed, a dilated right heart, and engorged vessels. Abnormal drainage of the *right-sided* pulmonary veins produces a thickened hilus, an "accessory hilus" (opacity caused by the confluence of the veins into, and projected over, the right atrium, a feature especially well seen on tomography), and inversion of the course of some of the venous trunks. Anomalous termination on the *left* is evidenced by pseudotumoral widening of the superior mediastinum to the left, due either to the innominate vein, the subclavian, or to persistent left-sided vena cava. Moreover, in certain localized segments, elevated pressure may result in the appearance of venous varicosities which, when pulsating, are good kymographic subjects.

Six illustrative instances are briefly discussed.

Fifteen roentgenograms. E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Hypervascularization in Chronic Inflammation Demonstrated by Angiography. Angiographic, Histopathologic, and Microangiographic Studies. Curt Lagergren, Åke Lindbom, and Gunnar Söderberg. Acta radiol. **49:** 441–452, June 1958. (Karolinska Sjukhuset, Stockholm, Sweden)

The authors present 4 cases which were considered both clinically and arteriographically to be neoplastic but in which the histologic examination revealed inflammatory processes. These were selected from a group of 150 cases of tumors and suspected tumors studied arteriographically.

The authors point out that hypervascularity discernible by angiography is not pathognomonic of tumors. Marked hypervascularization is sometimes associated with chronic inflammatory processes. In and contiguous to the affected zones the arteries are dilated and contrast medium passes from arteries to veins much more rapidly than in the surrounding tissues. This arteriovenous shunt probably occurs *via* large capillaries with diameters not exceeding 100 microns.

If, at arteriographic examination, pathologically changed tissue is highly vascular and contrast medium passes swiftly to the veins but no abnormal vessels can be observed in the affected area, angiographic differentiation between tumor and inflammatory process may not be possible.

The hypervascularization detected in skeletal metastases from carcinoma may be due to the round-cell infiltration that in some cases surrounds the tumor.

Arteriovenous shunts in varicose leg ulcers probably result from chronic inflammation and thus have the same etiology as similar shunts in other chronic inflammatory conditions attended by hypervascularization.

Fifteen roentgenograms; 5 photomicrographs.

THEODORE E. KEATS, M.D.
University of Missouri

Blood Circulation During and After Peripheral Arteriography. Experimental Study of the Effects of Triurol (Sodium Acetrizoate) and Hypaque (Sodium Diatrizoate). Percy Lindgren and Gunnar Törnell. Acta radiol. **49:** 425–440, June 1958. (Serafimerlasarettet, Stockholm, Sweden)

In experiments on cats the systemic blood pressure and the blood flow in skeletal muscle, intestine, and skin were recorded after intra-arterial injections—as in peripheral arteriography—of two tri-iodo-benzoic acid derivatives, sodium acetrizoate (Triurol) and sodium diatrizoate (Hypaque). Sodium acetrizoate produced marked vasodilatation and increase in blood flow lasting for ten to fifteen minutes. It had the same effect on the vessels of the muscles and cutaneous and intestinal vessels. Sodium diatrizoate produced a moderate increase in the blood flow of some one to two minutes duration and its vasodilator effect, moreover, was much less than that of sodium acetrizoate. The vasodilator action is attributed to a direct chemotoxic effect.

Nine figures; 1 table. THEODORE E. KEATS, M.D.
University of Missouri

Demonstration of Carotid Occlusion by Small Dose Arteriography. W. H. Oldendorf. Neurology **8:** 296–298, April 1958. (University of California Medical Center, Los Angeles, Calif.)

Many clinically suspected carotid artery occlusions are not studied angiographically because of possible effects of the contrast medium and the physical manipulation during arteriopuncture in a patient with known vascular disease. Therefore a simple technic using a

small needle and small amounts of medium was evolved.

A single 10 × 12-inch grid-cassette is positioned adjacent to the side of the head to be injected, so that the needle, inserted about 3 cm. below the carotid bifurcation, will be seen on the film. Local anesthesia is used. A sharp bevel 20 gauge 1.5-inch needle is inserted perpendicularly through the anterior and posterior walls of the artery, depressed about 45°, slowly withdrawn until the tip re-enters the arterial lumen, and then advanced 1 cm. upward in the lumen. Two cubic centimeters of 50 per cent Hypaque (in a 5 c.c. syringe) are injected over a period one to one and a half seconds. Immediately prior to completion of the injection, a single lateral exposure is made. This volume of Hypaque was found sufficient to visualize the entire carotid system. A definite segment of common carotid should be demonstrated to exclude injection directly into the external carotid.

This technic was used on 50 selected patients in a sixteen-month period. The internal carotid failed to fill in 9. There were no serious complications. A hematoma was visible in 1 case. The series is too small, however, to establish the safety of this procedure relative to full-scale arteriography.

Three cases are reported which illustrate the clinical value of small-dose arteriography in establishing or excluding internal carotid occlusion.

Three roentgenograms; 1 chart.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

A Follow-Up Study After Thorotrast Carotid Arteriography. A. Berrett and D. L. McRae. Canad. M. A. J. **78:** 916–921, June 15, 1958. (Montreal Neurological Institute, McGill University, Montreal, Que., Canada)

The authors were able to obtain a satisfactory follow-up on 134 of 136 patients in whom Thorotrast arteriography was done at the Montreal Neurological Institute between 1934 and 1950. The average length of follow-up was twelve and a half years, with a minimum of five years and a maximum of twenty-two. Either unilateral or bilateral carotid arteriography had been performed, an average of 25 c.c. of Thorotrast being used per examination.

Sixty-six of the 134 patients were dead, 51 of the disease that led to the carotid arteriography. In none of the 51 was there any suggestion of leukemia, aplastic anemia, or malignant tumor of liver or spleen. Ten patients died of accidents or other unrelated conditions following their discharge from the Institute. Three died of malignant disease other than brain tumor, but it is felt that this incidence is no greater than would be found in any population group of similar age and sex followed for an equal period.

Of the 68 living patients, 26 could be reached for detailed study. The most frequent complication in the series was the occurrence of thorotrastoma (14 per cent).

The authors suggest that, when Thorotrast arteriography is undertaken by the open method, the site of the needle be included in the lateral roentgenogram of the skull so that any extravascular injection or extravasation will be visualized. Deposition of contrast medium of any type around the carotid artery or within its wall may partly or completely occlude its lumen, thereby resulting in many of the neurological sequels attributed to the so-called toxicity of the contrast medium itself.

Minor hematological changes noted in 2 patients in this series are felt to be inconclusive, nor could any conclusions be drawn with regard to significant increase in cancer of the liver or spleen.

The authors regard this study as a preliminary one. Thorotrast is an extremely useful substance for the study of the long-term effect of small quantities of internally deposited radioactive material, but, in view of its long half-life, extended follow-ups are essential for its full evaluation.

Four roentgenograms; 2 photomicrographs.

Venography as a Guide to the Surgery of Stasis Ulcer of the Leg. Edward W. Friedman, E. Marvin Henken, and Edward D. Frank. New England J. Med. **258:** 1146–1149, June 5, 1958. (Beth Israel Hospital, Boston, Mass.)

Surgical therapy of stasis ulcers of the leg falls into two categories: (1) obliteration or removal of incompetent venous channels that produce chronic elevation of venous pressure in the region of the ulcer and (2) excision of the ulcer and adjacent tissues followed by skin grafting. The authors are concerned with the first of these. They believe that many incompetent venous channels escape detection on physical examination and that these are commonly responsible for recurrent ulcers. They advocate venography as a means of making surgery more effective.

Thirteen cases of persistent or recurrent leg ulcer were studied. Venography was done in all and treatment was in accord with the venographic findings. All of the group had failed to benefit from prolonged local therapy. Eleven had had intermittent ulcers for over a year and 4 of these for over sixteen years. Eight had undergone earlier surgery for varicose veins or leg ulceration.

In 10 of the 13 cases treated surgically on the basis of the guidance provided by venography the ulcers had remained healed, at the time of this report, for three to seven years, and in the 3 recurrences repeated venograms showed residual or new incompetent perforators, or both.

The method of venography is described. The contrast medium is injected through a vein on the dorsum of the foot, with the superficial circulation occluded, thereby permitting visualization of the deep venous and collateral circulation in the leg. Stereoscopic anteroposterior views are obtained. When this method is not possible, a superficial tributary to the saphenous system in the upper leg or thigh is exposed, divided, and cannulated in each direction. Injection is made into the upper catheter, to visualize the deep system in the knee area and evaluate the presence of incompetent communicating vessels. Following this, injection is performed in the distal catheter, demonstrating any incompetency in the superficial system.

Three roentgenograms; 1 table.

CAPT. BYRON G. BROGDON, M.D.
Lackland AFB, Texas

Angionephrography and Suprarenal Angiography: A Roentgenological Study of the Normal Kidney, Expansive Renal and Suprarenal Lesions and Renal Aneurysms. Gunnar Edsman. Acta radiol. Suppl. 155, 1957. (Roentgen Diagnostic Department I, Sahlgrenska Sjukhuset, Gothenburg, Sweden)

Only a review of the contents of this monograph is possible within the limits of an abstract. The author

has made a study of the normal anatomy and pathologic aspects of the kidney in a series of 965 patients examined by lumbar aortography. He introduces his report with a somewhat limited account of the technic and complications. This includes no discussion of faulty needle placement or injection or of the hazard to the femoral artery incident to the use of the Seldinger catheter.

The first chapter of the monograph deals with angionephrography of the normal kidney. Good discussions are given of the renal arterial and nephrographic phases, but the treatment of the venous phase is sketchy. A statistical analysis of the levels of origin of the renal vessels and their size is well done and there is a useful account of temporary arterial spasm causing incomplete filling of the vessels and the factors responsible for this.

Nine examples of unilateral ectopic kidney were included in the author's material and a short chapter is devoted to that anomaly and the associated accessory vessels. Horseshoe kidney is mentioned very briefly but no illustrations are given.

Malignant renal tumors are discussed in detail with consideration of the statistical features of the appearance, character, and timing of opacification of the arterial, capillary, and venous phases of the tumor circulation. In 80 cases of tumor, the author distinguished 75 as malignant, and 3 as solid tumor; 1 is unidentified because of its small size, and 1 could not be differentiated from cyst. Renal cysts and renal pelvic tumors are adequately illustrated.

The material on hydronephrosis includes demonstration of atrophy of the kidney and diminution of caliber of renal arteries in cases of intrarenal hydronephrosis but not in extrarenal hydronephrosis. The material on angiography in suprarenal abnormalities is excellent.

Sixty-seven figures; 18 tables.

WILLIAM R. EYLER, M.D.
The Henry Ford Hospital

Internal Mammary Venography. Robert Schobinger. J. Thoracic Surg. **35:** 692–695, May 1958. (Roswell Park Memorial Institute, Buffalo, N. Y.)

Intra-osseous venography has been used by the author to demonstrate the internal mammary vein pattern in a series of 50 unselected patients with primary breast disorders of benign and malignant nature. Included also were patients with postoperative metastatic carcinoma to axillary and supraclavicular nodes, and with or without involvement of the chest wall. The technic for the procedure is described and its advantages and limitations are discussed.

It was found that under normal conditions the injected contrast medium readily leaves the medullary cavity through several small veins which join a rather large venous channel on either side of the sternum. These veins follow a course parallel to the sternal edge and their anatomic location corresponds to the one occupied by the internal mammary veins. The caliber of these veins remains more or less equal, and filling in proximal direction can usually be followed up to their point of entry in the distal portion of the innominate veins; visualization in the distal direction may be variable.

The small branches which drain the medullary cavity of the sternum may not always immediately join the internal mammary veins but occasionally run in a longitudinal direction along the sternal border. It is important to recognize this fact and not to mistake these veins for narrowed segments of the internal mammary, especially if less dense filling of these latter veins has been obtained. There may, on the other hand, exist a real narrowing of the internal mammary vein itself, independent of any extrinsic pressure, which, as observed in several of the author's cases, usually occurs in the region of the third costal cartilage and mostly on the right. That such narrowing does not merely represent a roentgenographic artefact, due to insufficient filling of the vein with contrast material, has been confirmed by surgical exploration.

Since the internal mammary vessels are normally maintained in a more or less fixed position, their frank displacement by retro- or parasternal masses rarely occurs. There will rather be an encroachment upon the wall of these veins, with resulting narrowing of their lumen. In more advanced cases, there may be complete block of flow of blood within the internal mammary vein at the level of the lesion with accompanying development of collateral venous channels. Histologic investigation revealed that various lesions may produce partial or complete block of the internal mammary at any given level, *e.g.*, prominent parasternal fat pads, fibrous plaques following external irradiation, and metastatic cancer involving the internal mammary nodes.

In other words, internal mammary vein obstruction *per se* does not indicate carcinomatous involvement of internal mammary lymph nodes even if the presence of cancer (mostly of the breast) has definitely been established. Conversely, demonstration of a partial or complete block of the internal mammary vein in patients who are clinically "cured" may favor the existence of a hidden and unrecognized focus of metastatic carcinoma. Internal mammary venography enables the surgeon to obtain a biopsy at the site of possible metastatic involvement, either prior to surgery or after treatment. Not only a better selection of patients but a more adequate follow-up should be possible with initiation of proper secondary therapy at an earlier and thus more favorable time.

Two roentgenograms.

THE DIGESTIVE SYSTEM

X-Ray Findings in a Child with Candida Esophagitis. Herbert J. Kaufmann. New England J. Med. **258:** 1143–1146, June 5, 1958. (Boston University School of Medicine, Boston, Mass.)

The x-ray appearance of a case of *Candida albicans* infection of the lower esophagus in a four-year-old child is described. This is the first such report in American literature as well as the first recorded case in the pediatric age group. Radiographically there is a close resemblance to esophageal varices, but in this case the diagnosis was established at autopsy.

The risk of generalized candidiasis in patients treated for long periods with cortisone and antibiotics is again pointed out. It is in this group that the disease is most likely to occur. The child whose case is recorded here had received prolonged treatment with cortisone and subsequently with prednisone, for aplastic anemia, which eventually caused his death.

On the basis of the evidence available to date, the author summarizes the radiological findings in *Candida* esophagitis as follows: Early there is involvement of the lower portion of the esophagus while the upper half appears normal. If the disease progresses, the entire esophageal mucosa may be involved. Its outline is irregular, with protrusions and indentations of various sizes. Longitudinal folds may be preserved, but with

severe involvement are no longer detectable. In severe cases, also, narrowing of the esophageal lumen may be noted, again beginning in the inferior portion. Several cases reported have failed to show x-ray changes in the esophagus.

Two roentgenograms; 2 photomicrographs; 1 photograph.

CAPT. NEIL E. CROW, M.C.
Lackland AFB, Texas

Calcification in Gastrointestinal Malignancy. W. A. Matthews, J. E. Skandalakis, M. A. Mitchell, and H. S. Weens. Gastroenterology **34:** 959–968, June 1958. (Emory University School of Medicine, Atlanta, 3, Ga.)

Two new cases of calcification in gastrointestinal carcinoma are reported.

The first patient was a 59-year-old female complaining of anorexia, constipation, and weight loss. Occult blood was found in the stool. A gastrointestinal series revealed narrowing of the lumen throughout the midportion and distal part of the stomach. Bands of increased density due to thickening of the gastric wall were found along the lesser and greater curvatures. These contained numerous small, mottled calcium deposits. A subtotal gastrectomy was performed and histologic examination of the specimen revealed a mucinous adenocarcinoma with many calcium deposits filling the mucinous spaces.

The second patient, a 25-year-old male, complained of periumbilical and right lower quadrant pain and was found on physical examination to have a mass anterior to the rectum. A survey film of the abdomen revealed small mottled dense deposits in the course of the descending colon at the level of the iliac crest. A barium enema study showed these densities to be in a well defined filling defect with shelf-like edges, surrounding the lumen of descending colon. The patient died within a month and autopsy revealed mucinous adenocarcinoma with widespread metastases. The histologic examination showed calcium deposits in the mucinous spaces of the carcinoma.

A review of the literature revealed 8 previously reported cases of calcification in gastrointestinal cancers, 7 in the stomach and 1 in the rectum. All the neoplasms were mucinous carcinomas and were in the younger or middle-age group. Only 2 of the 10 patients were more than fifty years old and 6 were under forty years. The clinical course was often protracted.

Five roentgenograms; 2 photomicrographs; 1 photograph; 1 table.

H. GOULD, M.D.
St. Vincent's Hospital, New York

Calcification in Carcinoma of the Stomach. Olaf Petersen. Acta radiol. **49:** 416–418, June 1958. (Roentgen Department, University Hospital, Copenhagen, Denmark)

The author reports an additional case of calcification in carcinoma of the stomach. The patient was a farmer, 77 years of age, who had experienced increasing fatigue and dyspnea on exertion for three to four months prior to admission. Roentgen examination of the stomach showed a diffusion lesion with irregular dentate outlines, extending from the prepylorus almost up to the cardia. Calcifications of unusual appearance were noted in the superoposterior region of the abdomen, and films obtained before and after the administration of a contrast medium indicated that these were situated in a greatly thickened gastric wall.

The diagnosis of tumor was confirmed at operation. The gastric mucosa was greatly thickened, irregular, and ulcerated. In several regions the gastric wall was as much as 2 cm. thick; on section the tissue was whitish and partially transparent, containing numerous small granules of calcification.

The tumor in this case, as in all the published cases of gastric carcinoma with roentgen signs of calcification, was a mucinous adenocarcinoma. It is generally recognized that devitalized or dead tissue which is surrounded by living tissue has a tendency to calcify. The encased tissue is transformed into a hyaline material which biochemically is closely related to the mucinous substance found in mucoid carcinomas. In such areas the carbon dioxide tension is low and this is no doubt a factor in the chemical processes which lead to the deposition of calcium.

Three roentgenograms.

THEODORE E. KEATS, M.D.
University of Missouri

The Use of Amphetamine in Roentgenologic Evaluation of Pyloro-Duodenal Spasm. Piero Bistolfi. Radiol. med., Milan **44:** 521–545, June 1958. (In Italian) (Istituto di Radiologia dell'Università di Genova, Italy)

In the presence of pylorospasm, with subsequently contracted bulb, one may postulate the presence of ulcer, but it is often difficult, and sometimes impossible, to demonstrate the crater. Under such circumstances, several drugs have been employed in an attempt to relieve the spasm, as, for example, morphine, apomorphine, atropine, hyoscine, etc. These, however, usually produced side-reactions, unpleasant or dangerous to the patient and troublesome to the examiner (increased peristalsis).

In the present paper, the author reports on the use of amphetamine sulfate (the brand employed was Simpamine, produced by the Italian manufacturer Recordati), either 10 mg. parenterally or 5 mg. *per os*, for the average patient of 60 to 65 kg. weight. The spasmolytic effect was constant, beginning ten to thirty minutes after the intramuscular injection and twenty to forty minutes after ingestion of the tablet. No significant complications were encountered, and no modifications of peristalsis were noticed. In one patient, in whom the cap would not fill properly after the administration of amphetamine, surgical exploration disclosed the presence of local scarring with adhesions.

Fourteen observations are briefly illustrated.

Seventy-eight roentgenograms.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Peptic Ulceration Associated with Prednisolone Therapy. K. T. Evans. Brit. J. Radiol. **31:** 307–312, June 1958. (Hammersmith Hospital, London, W. 12, England)

In a series of 23 patients on long-term prednisolone therapy, 6 had radiological evidence of peptic ulceration. All of the ulcers demonstrated were in the prepyloric region or duodenal cap. They were quite large and were not associated with significant surrounding deformity, suggesting recent ulceration. Two of the patients were asymptomatic, and in the other cases the symptoms were mild.

Onset of symptoms after beginning of treatment varied from two weeks to thirteen months. Other

manifestations of corticoid therapy were not more evident in the ulcer cases. The average dose of prednisolone in the 23 cases was 20 mg. daily.

Increase in basal gastric secretion of hydrochloric acid and deficiency in mucus production are believed to be causative factors in peptic ulceration in these patients. Thirteen of the 23 patients had rheumatoid arthritis, and 5 of the 13 had peptic ulcers. A high incidence of peptic ulcers in patients with rheumatoid arthritis has been noted by Bauer (Proc. Conf. on Effects of Cortisone, December 10, 1951, Merck & Co., p. 56)

Twenty-three roentgenograms; 4 tables.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Hepatodiaphragmatic Interposition of Jejunum, Ileum, Cecum and Ascending Colon with Intestinal Obstruction. Report of a Case Corrected Surgically. David Wyatt Aiken. New England J. Med. **258:** 1192–1195, June 12, 1958. (4083d United States Air Force Hospital, Thule, Greenland)

Many cases of hepatodiaphragmatic interposition of the colon have been recorded and a few reports either have included or have been concerned solely with interposition of the small intestine. Surgical intervention has seldom been required. The case presented here is a unique one of high intestinal obstruction caused by hepatodiaphragmatic interposition of the cecum, the ascending colon, and most of the small intestine, corrected by surgery.

A fourteen-month-old boy was admitted to a U. S. Air Force Hospital with signs of low-grade intestinal obstruction. He did not respond to conservative treatment, and surgical intervention was planned. The preoperative roentgenogram showed the intestine above the liver, the right dome of the diaphragm at the level of the third rib, the ascending colon lateral to the liver, and the stomach dilated, with a fluid level. At operation the stomach was found to be partially decompressed, whereas the duodeum was dilated with fluid. From the ligament of Treitz a dilated, fluid-filled, tense jejunum coursed directly to the right side of the abdomen, as though it had been pulled there, continued to the posterior border of the right lobe of the liver in the "lumbar gutter," and thence disappeared behind the liver. The obstruction was nearly complete. Beside the limb of the jejunum, normal transverse colon emerged from behind (and lateral to) the liver. This latter organ showed no marked downward displacement. The ascending colon, cecum, appendix, and entire small intestine below the first 6 to 8 cm. of jejunum were all interposed between the liver and the right leaf of the diaphragm. By means of gentle traction the small bowel and colon were returned to their normal position. No abnormality of the diaphragm or signs of a hernia were noted. The child made an uneventful postoperative recovery and one year later was doing well, without further gastrointestinal difficulty.

Four roentgenograms. ALFRED O. MILLER, M.D.
Louisville, Ky.

Acute Pancreatitis: A Clinical Review of 72 Attacks Occurring in 54 Patients. Paul L. Shallenberger and David F. Kapp. Ann. Int. Med. **48:** 1185–1193, June 1958. (Guthrie Clinic, Sayre, Penna.)

Records of all patients in whom a diagnosis of acute pancreatitis was made during the period 1940–1955 at the Guthrie Clinic were reviewed. Proof of diagnosis was considered adequate only if, in addition to the clinical history, one or more of the following criteria were met: (1) elevated serum amylase, (2) elevated serum lipase, (3) surgical or autopsy demonstration of either hemorrhagic pancreatitis or pancreatic fat necrosis. On this basis, a series of 72 attacks in 54 patients was assembled.

Pain varying from moderate to severe was the chief complaint of 100 per cent of the patients. The majority had mid- or right epigastric pain of a nonrelenting, boring character, with frequent radiation to the subscapular area. Nausea and/or vomiting occurred in all but 9 attacks. Diarrhea during an acute episode of pancreatitis was not observed.

The precipitating cause was a heavy or fatty meal in 24 attacks. Twelve episodes were ushered in on the heels of a drinking spree. One case was the direct result of trauma.

The status of the extrahepatic biliary tree at the time of the initially observed attack was determined by x-ray, operation, or autopsy in 44 of the 54 patients; 21 had a normal patent biliary tree without stones, while 23 had evidence of past or present biliary tract disease.

The two conditions most frequently confused with pancreatitis were acute biliary colic and penetrating or perforated peptic ulcer.

Fever of significant degree was noted in only 31 of 72 attacks (43 per cent) at the time of admission. Tenderness was present in 66 instances, with associated rigidity in 24.

In the absence of pancreatic calculi, which are pathognomonic of existing chronic pancreatitis, two radiologic findings should alert the examiner to the possibility of the diagnosis of acute pancreatitis; (1) localized small bowel ileus as seen on the abdominal "scout film"; (2) segmental or "plate-like" atelectasis in the basilar lung fields on the routine admission chest films. Of 35 admission abdominal scout films, 11 revealed a local segment of dilated small bowel, usually in the left upper quadrant; 1 revealed right upper quadrant calculi, presumed to be gallstones, and 1 revealed pancreatic calculi.

Twenty-one of 54 patients had elevated serum bilirubin levels at some time during the course of an acute attack of pancreatitis. Glycosuria was noted in only 18 of the 72 attacks, whereas hyperglycemia was noted in 38. In 9 of the 45 survivors permanent diabetes mellitus developed.

Fifty-two attacks were managed solely by medical treatment, and 5 of the patients died as a direct result of pancreatitis. Twenty patients were operated on at some time during their hospitalization and 3 of these died in the postoperative period. Five of the operations were emergency laparotomies, done because the correct diagnosis had not been considered preoperatively.

When the diagnosis of acute pancreatitis has been made with reasonable certainty, medical management is to be preferred. Surgery should be reserved for complications or the correction of associated biliary tract disease and, if the patient's condition permits, should be delayed well into convalescence.

Four roentgenograms; 1 table.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

The Papilla of Vater and Distal Portions of the Common Bile Duct and Duct of Wirsung. Herbert F. Newman, Sidney B. Weinberg, Ernest B. Newman, and Jane D. Northup. Surg., Gynec. & Obst. **106:** 687–694, June 1958. (Beth Israel Hospital, New York, N. Y.)

An investigation was undertaken to study radiologically the normal anatomy of the major biliary and pancreatic ducts in their distal portions, with particular emphasis on relationship to the papilla of Vater. Eighty human cadavers were examined within forty-eight hours after death. Roentgenograms were taken in 52 cases without gross evidence of pancreatic or biliary disease, and in 5 cases of chronic pancreatitis.

Iodized oil was injected simultaneously into the common bile duct and into the pancreatic duct of Wirsung *via* a transected pancreas with just enough force to cause a free flow of the material from the papilla of Vater. Roentgenograms were taken and from these tracings were made of the distal portions of the common bile duct and the major pancreatic duct down to their exit into the duodenum. The length of the papilla of Vater, previously measured directly *via* the opened duodenum, was inscribed on each tracing.

In the fresh specimens the papilla was found to be a well circumscribed mucosal elevation, the shape of a Quonset hut, with an average length of 11.7 mm. and a width of 5.2 mm. It usually forms the anterolateral wall of the distal portion of the common duct and of the ampulla. The size of the papilla is not a criterion of disease. The largest normal papilla was 21.0 mm. long and 10.0 mm. wide. A normal papilla could not be palpated through the unopened duodenum. In the authors' clinical experience, a palpable papilla was the site of papillitis, hypertrophy, or neoplasm.

The following relationships of the common bile duct, the pancreatic duct of Wirsung, and the papilla of Vater were observed: In 1 case the duct of Wirsung emptied separately through a lesser papilla, and in all of the remaining, both it and the common duct opened on the papilla of Vater. In 5 of the latter, separate openings could be visualized at the papilla. An ampulla, or common anatomical channel, was present in 88 per cent of the normal material. In 80 per cent of the specimens the ampulla was 3 or more mm. in depth when measured from the surface of the papilla to the septum between the two ducts.

Cholangiography in the cadavers revealed a funneling of the distal portion of the common duct prior to its entrance into the duodenal window, similar to that observed in the living. The duct lumen is usually narrowest at some point proximal to the papilla, and may widen if an ampulla is present. In 34 per cent of the specimens the narrowest portion of the common duct lay within the papilla.

The duct of Wirsung maintains a fairly constant diameter through the body, neck, and head of the pancreas until it approaches the papilla, where it may narrow slightly, but the funneling seen in the common duct occurs infrequently.

In 1 specimen there was a diverticulum arising in its usual location from the medial aspect of the second part of the duodenum. Apparently the duct of Wirsung bore a close relationship to the posterior surface of this diverticulum. Diverticulectomy in such a case would be fraught with danger.

Fifty-six tracings showing the relationship between the common bile duct, the duct of Wirsung, and the papilla of Vater are reproduced.

Five tables. MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Oral Cholecystography: An Evaluation of Its Accuracy. Hillier L. Baker, Jr., and John R. Hodgson. Gastroenterology **34:** 1137–1145, June 1958. (Mayo Clinic, Rochester, Minn.)

The authors have reviewed two series of cholecystographic examinations performed at the Mayo Clinic in 1950 and 1955, respectively, in order to evaluate the accuracy of the procedure in the light of improvements in technic and media since Kirklin's 1933 study with sodium tetraiodophenolphthalein (J.A.M.A. **101:** 2103, 1933. Abst. in Radiology **22:** 256, 1934). Because the purpose was to correlate surgical and pathologic findings with the cholecystographic data, the records of all abdominal operations performed at the Clinic in the two years were reviewed: 1,223 examinations with Priodax were performed in 1950, and 1,180 examinations with Teridax in 1955.

It was found that 2.7 per cent of the diagnoses in 1950 and 2.4 per cent of those in 1955 were in error. Kirklin, in 732 examinations, had had 5 per cent erroneous diagnoses. On the basis of the three series, it is concluded that the diagnostic accuracy of cholecystography is within the range of 95 to 98 per cent.

The authors' best results were in the diagnosis of calculi, polyps, papillomas, and adenomas, where the accuracy was 99.1 per cent. The incidence of inaccuracy increased when interpretation was based solely on gallbladder density; a diagnosis of "poorly functioning gallbladder" was attended by a 9.1 per cent error in 1950. This diagnosis was eliminated in 1955, when the denser medium, Teridax, was employed.

Diagnoses of a normally functioning gallbladder showed an error of 6.2 per cent and 5.2 per cent in 1950 and 1955, respectively. Kirklin and others had held that this error was from 10 to 20 per cent.

Nonfunctioning gallbladders were found to be normal in 3 per cent of the cases thus diagnosed, and a review indicated that this represents an unavoidable error.

The authors believe that about one-third of the errors could be eliminated by enforcement of more rigid control in technic or interpretation. Use of the more dense Teridax did not obscure tiny calculi or render visible abnormal gallbladders not containing stones.

One chart; 2 tables. JOHN C. POWERS, M.D.
St. Vincent's Hospital, New York

Eccentric Contractions of the Gallbladder in Cholecystography. Lars Andrén and Georg Theander. Acta radiol. **49:** 464–470, June 1958. (Allmänna Sjukhuset, Malmö, Sweden)

The authors observed eccentric variable contractions of the gallbladder in 8 per cent of 1,351 cholecystographies in which filling was obtained. These contractions, when marked, may result in local narrowing of the gallbladder so that it becomes tortuous or lobate in shape. Large circumscribed indentations may be seen, resembling those produced by tumors in or outside the wall of the gallbladder. A longitudinal or spiral folding may occur, and the gallbladder may appear to be twisted about its long axis. Again, the eccentric contractions may produce only shallow indentations or

flattening of parts of the gallbladder wall. The dynamic nature of the phenomenon is apparent on fluoroscopy or serial roentgenography. The shape of the gallbladder is then seen to alter spontaneously, on change in posture, or on the application of pressure.

In this study eccentric contractions of the gallbladder occurred only after the use of media containing iopanoic acid (Telepaque) and its sodium salt (Bilijodon-Natrium), which would suggest that they were produced by the contrast material. This assumption is supported by the observation that the phenomenon occurred almost exclusively in well filled gallbladders, *i.e.*, in gallbladders containing contrast medium in high concentration. It appears reasonable to assume that local irritation of the wall by the contrast material may be responsible.

Eccentric contractions are more common in women than in men, particularly between the ages of thirty and fifty years. If this phenomenon, as suggested, is caused by the local action of the cholecystographic medium, its difference in frequency with sex might possibly be due to some difference in the sensibility or motility of the gallbladder, which might in turn be related to the sex difference in gallbladder disease. An interrelationship between the susceptibility to eccentric contractions and the liability to gallbladder disease might also be responsible for the overrepresentation of eccentric contractions of the gallbladder in women between the ages of thirty and fifty.

Twenty-five roentgenograms; 1 diagram; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

Hamartoma of the Gall Bladder in a Child. Richard C. Brown and Richard J. Brown. J. Pediat. **52:** 319–323, March 1958. (113 E. Williams St., Owosso, Mich.)

The authors report a case of hamartoma of the gallbladder occurring in a seven-year-old child with quadriplegia believed to be due to a diffuse brain sclerosis associated with demyelinization of the white matter. In June 1955, an egg-sized mass was felt in the abdomen near the hepatic flexure of the colon. Over the next month this became enlarged to the size of a grapefruit. Intravenous pyelograms showed normal and calyceal outlines, but irregular clusters of calcium were visible in the region of the right kidney, in anteroposterior views. Roentgenograms of the chest and skull were normal. A malignant renal, adrenal, or retroperitoneal tumor was suspected but, because of the incurable nature and advanced stage of the brain degeneration, exploration was thought unwarranted.

During the next six months the mass continued to enlarge, finally reaching the left midclavicular line and the iliac crest; according to the mother, it "broke" on Jan. 3, 1956. On examination the definite mass was no longer palpable, but the abdomen was distended and diffusely tender, with signs of intra-abdominal fluid. Acute symptoms subsided with conservative treatment and, in April, 1,000 c.c. of fluid was aspirated by abdominal paracentesis. Careful study of a centrifuged sample of the fluid revealed no tumor cells.

Review of all roentgenograms at this time placed new emphasis on a lateral film showing the calcifications clustered rather more anteriorly than might be expected for a mass originating in the kidney-adrenal area. Cholecystography was attempted, but no medium was visualized in the gallbladder after single and double doses of Telepaque. Surgical exploration disclosed a gallbladder filled with what appeared to be a mucoid type of carcinoma, with large nodes along the cystic and common ducts. Cholecystectomy was performed. On pathologic examination, the initial impression of adenocarcinoma of the gallbladder was changed to hamartoma.

No previous report of gallbladder hamartoma could be found in the literature. There is believed to be no correlation between the hamartoma and the patient's brain degeneration. Observation for eighteen months had shown no evidence of recurrence or metastasis.

Three roentgenograms; 1 photograph; 1 photomicrograph.

Polypoid Cholesterolosis of the Gallbladder: A Clinical and Radiological Evaluation. Robert G. Fraser, Carleton B. Peirce, and Patrick J. Fitzgerald. J. Canad. A. Radiologists **9:** 15–25, June 1958. (Royal Victoria Hospital, Montreal, Que., Canada)

Cholesterolosis, in a considerable proportion of cases, is a radiologically diagnosable disease, and is potentially a symptom-producing lesion. Pathologically, it is characterized by an accumulation of abnormal amounts of lipoid, chiefly cholesterol and its esters, in the wall of the gallbladder, both intracellular and stromal. The deposits vary markedly in size, from diffuse speckling of the mucosa to polypoid masses protruding into the gallbladder lumen. A series of 23 cases of the polypoid type is reported here.

Clinically cholesterolosis is similar to cholecystitis or cholelithiasis. The incidence reported on pathological studies by other authors is about 23 per cent of all diseased gallbladders. The roentgen appearance is that of multiple irregular filling defects in the contrast-filled gallbladder. Unlike the defects due to calculi, the position of these is constant. Spot films are of significant aid in demonstrating these polypoid defects. Gallbladders usually show good concentration of the medium and a rapid emptying response to the fat meal. In differential diagnosis, calculi and polyps are to be considered.

Fifteen roentgenograms; 1 photomicrograph; 3 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

Television Radioscopy During Operations on the Biliary Passages. P. Mallet-Guy. Surg., Gynec. & Obst. **106:** 747–748, June 1958. (Lyons, France)

In 1952, the author described a combined manometric and roentgenographic technic for examination of the biliary passages during operation (Surg., Gynec. & Obst. **94:** 385, 1952. Abst. in Radiology **60:** 311, 1953). This procedure has now been used in 3,000 cases and in the past year has been supplemented by television radioscopy.

A portable 70-kv x-ray machine placed under the operating table sends rays through the patient, which are picked up over the table by a composite image amplifier television camera, which then transmits the image to television screens. This affords the surgeon immediate and personal information complementing the manometric and radiologic findings. It is felt to provide new precision in the investigation of stones in the common duct, analysis of dystonia of the sphincter of Oddi, and early growths of the ampulla of Vater.

Two photographs.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

HERNIA

About Diaphragmatic Hernias. E. de Arzua Zulaica. Rev. clín. españ. **69:** 217–224, May 31, 1958. (In Spanish) (Bilbao, Spain)

This is a comprehensive review and analysis of 46 patients with esophageal hiatus hernia encountered by the author in his practice. An enlightened discussion and detailed summary of findings is presented.

Among several other interesting observations, the frequent association of hiatus hernia and cholelithiasis is commented upon. Since both processes tend to affect obese women of middle and advanced age, the association has to be considered coincidental. Nevertheless, the percentage of association requires that, when one is found, the other should be sought.

The relatively large number of patients with gas pains suggests a relation between increased abdominal pressure and hiatus hernia. Symptoms in this series seemed otherwise to have little individuality and were generally nonspecific.

The demonstration of hiatus hernia was best accomplished by the author with the patient in prone Trendelenburg (procumbent) position or variations of it.

It is pointed out that esophageal reflux may produce symptoms suggesting hiatus hernia, but that this often occurs without hiatus hernia and may also persist after surgical repair of a hernia.

Treatment is discussed at some length; it is medical in most cases. Surgical indications are: bleeding, which is sometimes caused by constriction of the collar around the hernia, narrowing from esophagitis, strangulation, or an associated lesion, such as ulcer or cancer. Some believe that in the presence of gallstones cholecystectomy will correct or reduce the hiatus hernia symptoms. This was experienced in one case in the author's series, but in others dyspeptic symptoms continued postoperatively.

Eighteen roentgenograms.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

THE MUSCULOSKELETAL SYSTEM

Skeletal Lesions in Leukaemia in Children. S. Brünner, C. E. Gudbjerg, and Torben Iversen. Acta radiol. **49:** 419–424, June 1958. (Rigshospitalet, University Hospital, Copenhagen, Denmark)

The authors review the skeletal lesions in leukemia in childhood as seen in 32 children with this disease admitted to their hospital. Leukemic lesions of bone were divided into four roentgenologic types with the following predominant characteristics:

(1) *Translucent zones in the metaphyses.* These vary from 1 to 7 mm. in width and as a rule are bilateral; they usually affect the distal part of the femur and the proximal part of the tibia or the distal ends of the radius and ulna. They have been seen as early as four weeks after the first clinical signs of acute leukemia. These translucent bands are caused by focal skeletal destruction by proliferating leukemic tissue. They are not, however, specific for leukemia.

(2) *Destructive changes* appear in the roentgenogram partly as focal translucencies in the spongiosa and cortex, including the epiphyses, and partly as diffuse osteoporosis involving the entire bone. Destructive changes may be encountered in any of the bones, but are seen particularly in the pelvis and vertebral bodies, in which latter situation they may give rise to collapse and spontaneous fractures. The lesions are due to infiltration by the leukemic tissue and erosion of the bone.

(3) *Subperiosteal new bone formation* is manifest in the roentgenogram as a linear density parallel to and separated from the bone, spreading segmentally or along the entire length of the shaft. In rare cases, radiating spicules may be evident. The explanation of these changes is presumably that the proliferating leukemic tissue elevates the periosteum, the osteoblasts of which form a new layer of bony tissue around the original bone.

(4) *Osteosclerosis* may be diffuse in one bone or generalized. Its pathogenesis is in doubt.

Nearly half the authors' patients had bone pain, and all but one of these had skeletal changes. The lesions were often present within the first four months after the onset of clinical manifestations. The effect of treatment with antileukemic drugs upon the bone changes varies from patient to patient.

Six roentgenograms; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

Metastatic Embryonal Rhabdomyosarcoma in the Growing Skeleton: Clinical, Radiographic, and Microscopic Features. John Caffey and Dorothy H. Andersen. J. Dis. Child. **95:** 581–600, June 1958. (Babies Hospital, New York 32, N. Y.)

Five case reports of embryonal rhabdomyosarcoma in children with scattered metastases in the skeleton form the bulk of this paper. The first sign of disease in 3 patients was the appearance of the primary swellings —located in the dorsal thoracic wall in one, in the foot in another, and in the orbit in the third. In the 2 remaining patients, pain and limitation of motion at the sites of secondary tumors in the skeleton—in a shoulder in one case and in the lumbar spine in the second—were the initial clinical manifestations. In both of these patients, in retrospect, primary tumors were present early—one near an ankle and the second in the foot—but had been overlooked.

The authors believe that they are the first to describe the radiographic appearances in the skeletal metastases of rhabdomyosarcoma. The changes were almost wholly destructive, resembling the findings in neuroblastoma both in the character of the single lesions and in their pattern of distribution in different bones. The primary tumors occurring in soft tissues do not show radiographic evidence of direct extension to contiguous bones despite the wide dissemination in the skeleton at other sites.

The radiographic findings require differentiation from leukemic destruction, metastatic neuroblastoma, metastases from other neoplasms, and occasionally eosinophilic granuloma in a single site. While the roentgen picture is not sufficiently characteristic for reliable differentiation, additional information from clinical and blood studies will usually make possible a correct diagnosis. The most difficult differential problem concerns neuroblastoma. That tumor, however, does not appear to develop in skeletal muscle as does rhabdomyosarcoma. Frequently biopsy will be necessary for final diagnosis, but even microscopic changes may be uncertain, owing to the primitive character of the poorly differentiated myoblasts and their variations.

Radiotherapy was effective in 4 of the authors' cases, with improvement in pain, tenderness, and limitation of motion, and shrinkage of masses. In all instances,

however, the tumor recurred and further irradiation was ineffective. New skeletal tumors appeared and grew rapidly in sites of previous irradiation.

Twenty-four roentgenograms; 8 photomicrographs; 2 photographs. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Metaphyseal Dysostosis Resembling Vitamin D-Refractory Rickets. Robert Evans and John Caffey. J. Dis. Child. **95**: 640–648, June 1958. (Babies Hospital, New York 32, N. Y.)

A case is reported of a peculiar and unclassified disorder of the metaphyses with radiographic, clinical, and microscopic features, mimicking vitamin D-refractory rickets. The patient, a girl twenty-two months of age, had seemed quite normal until she began to walk, when a waddling gait and bowleg deformity were apparent. Roentgenograms revealed changes in the metaphyseal zones of the long tubular bones similar to those seen in active rickets. Epiphyseal ossification centers were well formed and normally developed. Abnormally deep radiolucent zones extended irregularly from the epiphyseal cartilages into the proximal femoral metaphyses but were limited at several sites by a narrow peripheral zone of provisional calcification. The radiolucent epiphyseal cartilage plates at the distal femurs and proximal tibias were excessively deep and their junctions with the bony metaphyses were irregular in outline. In contrast, the edges of the epiphyseal ossification centers appeared normal.

Laboratory findings were essentially normal, including serum alkaline phosphatase and all renal studies. Biopsy of bone at one of the costochondral junctions was consistent microscopically with active rickets. A later study showed low serum CO_2 and increased urinary excretion of calcium. A therapeutic trial of vitamin D resulted in return of these values to normal and prompt improvement in the appearance of the metaphyses, but the metaphyseal abnormalities subsequently became more pronounced and at thirty months the patient was readmitted to the hospital with the skeletal lesions unimproved. Greatly increased doses of vitamin D, up to 150,000 units per day were now given, followed in about four months by unmistakable evidence of vitamin D intoxication. Some improvement in the metaphyseal deformities did occur, and over the next few years the changes in the metaphyses tended to come and go but never completely disappeared.

The term "metaphyseal dysostosis" seems currently suitable for the abnormal metaphyseal lesions described here, although it is admitted that the cause is not known and that other closely related disease entities may be included in this term. Some authors believe metaphyseal dysostosis is a form of atypical dyschondroplasia. For the present, it is important that physicians be aware of a disease which may resemble vitamin D-refractory rickets clinically and radiographically, in order that they may avoid the administration of toxic quantities of vitamin D to such patients.

Twelve roentgenograms; 2 photographs.
JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Roentgenological Evidence of Injury to the Soft Tissues of the Cervical Spine. D. G. Wollin. J. Canad. A. Radiologists **9**: 32–35, June 1958. (Toronto General Hospital, Toronto, Ont., Canada)

The author describes four types of injury to the soft tissues (ligaments and intervertebral disks) of the cervical spine: (1) bilateral forward dislocation of the atlas, (2) unilateral forward dislocation of the atlas, (3) flexion deformity, (4) extension deformity.

Bilateral forward dislocation of the atlas is more commonly postinfectious than traumatic. The author collected 11 cases associated with injury, in 6 of which there were associated bony abnormalities of the cervical spine or foramen magnum. An underlying congenital weakening of the transverse ligament of the atlas is suggested. There was no correlation between the degree of displacement and the presence of cord compression.

Unilateral forward dislocation of the atlas on the axis (rotation deformity) varies in degree and resultant disability. Roentgenograms reveal displacement of the spine of C-2 to one side in relation to its normal alignment with the posterior arch of the atlas and the base of the skull.

Flexion deformities of the cervical spine are the most frequent sequel of injury. They are of two types. In the first, the body of one vertebra is tilted on that of the vertebra below, producing a localized kyphosis. The spines of the vertebrae at the site of the kyphosis are separated and films in flexion and extension show no evidence of movement in these two segments. This deformity has been attributed to rupture of the interspinous ligaments. In the second type of flexion deformity, the horizontal movement of a vertebral body on the one below is demonstrated on bending films. Here, in addition to rupture of the intraspinous ligament, one must postulate a fracture through the intervertebral disk.

The extension deformity is caused by violent hyperextension of the neck with resulting rupture of the anterior longitudinal ligament. A fracture of the intervertebral disk is present, and quadriplegia and death due to damage to the cord may ensue. Roentgenograms in extension reveal retrodisplacement of the vertebral body.

Eight roentgenograms; 4 photographs.
J. S. ARAJ, M.D.
Toledo, Ohio

Localized Osteochondritis of the Spine. Norman M. Brown. J. Canad. A. Radiologists **9**: 26–31, June 1958. (1414 Drummond St., Montreal, Que., Canada)

The author reports 3 cases of localized osteochondritis of the dorsolumbar spine, which he considers as another, but less well recognized form of Scheuermann's disease. The various theories as to the etiology of Scheuermann's disease are briefly discussed.

The 3 patients were girls from ten to sixteen years of age. Two had pain which followed trauma, while the third was asymptomatic. In all of them roentgenograms disclosed some narrowing of the disk space with localized defects at the anterior vertebral margins. Symptomatic and radiographic improvement was noted after a period of restriction of strenuous activity.

Differentiation from tuberculosis is important. The following factors are significant: (1) There is no paravertebral abscess. (2) The vertebral defect has a characteristic punched-out appearance. (3) Schmorl's nodes or other evidence of vertebral epiphysitis may be present. (4) Skin tests, laboratory studies, and chest roentgenograms are normal.

Eight roentgenograms. J. S. ARAJ, M.D.
Toledo, Ohio

Osteochondritis of the Greater Trochanteric Epiphysis. Thomas D. Hall. J. Bone & Joint Surg. **40-A**: 644–646, June 1958. (30 N. Michigan Ave., Chicago, Ill.)

Osteochondritis of the greater trochanteric epiphysis is an apparently rare lesion which occurs during adolescence and is similar in etiology and pathology to osteochondritis in other epiphyses. The condition has been called Monde's disease, after an original report in the German literature by Felix Monde, but the true credit belongs to Felix Mandl.

The author reports a case in a ten-year-old obese boy who was first seen with a waddling gait and pain in both hips. He had a bilateral pes planovalgus, but corrective shoes did not reduce his complaints. Compression over the femoral trochanters caused pain, and roentgenograms disclosed widening of the epiphyseal line, sclerosis on both sides of the epiphyseal plate, and fragmentation of the superior pole of the greater trochanter in each extremity. The basal metabolism was −11. Restricted activity was advised, and a follow-up eight months later revealed no abnormality of gait and absence of pain and of fragmentation. There is no mention of further studies of thyroid function or of possible thyroid treatment.

Five roentgenograms.

LAWRENCE A. POST, M.D.
University of California, S. F.

Ossification of the Distal Femoral Epiphysis. John Caffey, Samuel H. Madell, Charles Royer, and Pablo Morales. J. Bone & Joint Surg. **40-A**: 647–654, June 1958. (J. C., Babies Hospital, New York 32, N. Y.)

Because the authors were impressed by the frequency of irregular marginal ossification of the distal femoral epiphyses in children, roentgenograms of the knees of 147 children from three to thirteen years of age who had been referred for examination of a different body part were studied. Anteroposterior, lateral, and tunnel projections were obtained in each case. Marginal irregularities were quite common, particularly in younger children, where there was a positive incidence above 70 per cent below the age of five years. The overall incidence was 66 per cent in the boys and 41 per cent in the girls. The changes were often bilateral, but not always symmetrical.

The irregularity varied in degree from slight roughening of the margin to localized indentations and, in some cases, independent islands of bone within these craters. The latter change was not unusual, and presented a roentgen appearance identical to the change in osteochondritis dissecans. Follow-up on 2 of these asymptomatic children showed spontaneous disappearance of the defects.

The authors conclude that while osteochondritis dissecans in the femora of children can occur, it is much less frequent than this normal variation in ossification which simulates it. The value of the tunnel view in demonstrating the changes is stressed.

Twelve roentgenograms; 2 diagrams; 1 table.

LAWRENCE A. POST, M.D.
University of California, S. F.

Legg-Calvé-Perthes' Disease: A Study of Late Results. David L. Evans. J. Bone & Joint Surg. **40-B**: 168–181, May 1958. (Southend General Hospital, Southend, Essex, England)

P. F. Møller in 1926 reviewed 75 hips with healed Perthes' disease and found significant symptoms of osteoarthritis in 21.6 per cent of the patients. Legg (1927) followed 46 cases for more than ten years and concluded that, though most patients would have minor symptoms of this disorder and more than half would show a persistent limp, none would be incapacitated. Conflicting reports have been published by others.

In view of the differences of opinion as to the late results a study was made of 52 patients treated for Legg-Calvé-Perthes' disease at the Royal National Orthopaedic Hospital. Thirty-nine of the series were boys and 13 girls. The right hip was affected in 28 patients, the left in 24. The duration of symptoms before treatment was begun varied from one to thirty-six months, averaging six months. The average duration of treatment was twenty-five months—ten months traction, followed by fifteen months in a caliper. The follow-up varied from ten to thirty-six years.

The results of treatment—good, fair, and poor—have been assessed solely on the final shape of the femoral head, but symptoms and mobility have been correlated with this. "Good heads" showed a circular outline on both anteroposterior and sitting lateral views of the hip, with the head set squarely on the femoral neck and the acetabulum normal. Comparison with the normal hip, however, revealed some evidence of preexisting Perthes' disease, as enlargement of the femoral head, decreased height of the epiphysis, slight subluxation, shortening, or broadening of the femoral neck. In "fair heads" the outline was elliptical in either one or both projections but smooth and regular. "Poor heads" showed a deformed outline in both projections and all showed varying degrees of osteoarthritis and backward displacement of the head and neck. Clinical results paralleled the roentgen findings. The results for the series were as follows:

Good (15 cases): Thirteen patients had full mobility and 2 had restriction of movement in one direction only.

Fair (21 cases): Sixteen patients had no symptoms, 3 ignored them, and 2 made concessions on this account. Eleven patients had full mobility, 9 had limitation of movement in one direction, and 1 had limitation in two directions.

Poor (16 cases): Four patients had no symptoms, 9 ignored them, and 3 made concessions on this account. One patient had full mobility, 3 patients had limitation in one direction, 1 patient in two directions, and 11 patients in three or more directions.

The age at onset of the disease is important. Except in one case, a good result did not occur with onset after six years, and with a single exception the result was poor if the age at onset was over eight years. Whereas three-quarters of the boys showed good or fair heads and one-quarter poor heads, less than half the girls obtained good or fair heads and over half had poor heads.

In the present material the extremes previously reported did not occur. Most patients had either a fair or good result. Radiography appeared to be the best method for following developments.

Thirty-two roentgenograms; 3 graphs; 2 tables.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Sarcoidosis of Hands. Patrick FitzGerald and F. O. C. Meenan. J. Bone & Joint Surg. **40-B**: 256–261, May 1958. (St. Vincent's Hospital, Dublin, Ireland)

This is a presentation of a case followed from 1951

through 1957. In 1943, at the age of fourteen, the patient had first experienced burning pain and swelling of the middle finger of the left hand, leading to an amputation through the middle phalanx. In 1945 the same symptoms appeared in the corresponding finger of the right hand, and it too was partially amputated, in 1946. From inquiries it was clear that the condition had originally been treated as a fungus infection, though there had been no purulent discharge except for a short time from the right ring finger. The opportunity for biopsy afforded by the amputations had been missed.

In June 1951, a diagnosis of Boeck's sarcoid affecting the fingers was established mainly on the basis of biopsy of the skin and the radiographic appearance of the fingers. Roentgenograms showed the coarse expansion of the trabecular structure characteristic of sarcoidosis. The pattern of bone damage closely followed the superficial changes. There was almost complete disappearance of the phalanges in the tips of the severely involved right ring and left little fingers.

In June 1951 the patient was given 600 milligrams hydroxy-phenyl-cinchoninic acid daily for ten days. In March 1952, 100,000 units of vitamin D_2 (calciferol) daily were prescribed. Because of nausea and vomiting, the dose was reduced to 50,000 units daily in the following month, and this dosage was continued for six months. Treatment was then stopped.

A radiograph taken in 1957 showed improvement in the bony structure. At the same time the patient wrote to say that her hands remained healthy and that she had resumed work as a typist.

Three roentgenograms; 2 colored photomicrographs; 2 colored photographs; 1 diagram.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Osteopetrosis with Syndactyly: A Morphological Variant of Albers-Schönberg's Disease. A. S. Truswell. J. Bone & Joint Surg. **40-B:** 208–218, May 1958. (University of Cape Town, Cape Town, Union of South Africa)

The author presents 2 cases to be added to 5 others found in the literature featuring the syndrome of syndactyly with osteopetrosis.

The outstanding feature of this syndrome is the association of syndactyly with osteopetrosis, but in addition there have occurred: (1) atrophy of the distal phalanges; (2) thickening of the shafts of metacarpals and metatarsals; (3) thickening of the skull vault, facial bones and mandible, producing a mild degree of leontiasis ossea; (4) marked thickening of the clavicle.

In view of the prior cases reported in the literature and the addition of the present cases the author feels that there is sufficient reason to consider this combination a distinct morphological variety of osteopetrosis rather than a coincidental developmental finding.

Fourteen roentgenograms; 4 photographs.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Stress Fractures of the Tibia in Athletes or "Shin Soreness." M. B. Devas. J. Bone & Joint Surg. **40-B:** 227–239, May 1958. (12 Richmond Road, Bexhill on Sea, Sussex, England)

"Shin soreness" and "shin splints" are terms used by athletes to describe a painful condition of the shin which can seriously interfere with training and performance in the various forms of running. The purpose of this paper is to show that "shin soreness" is caused by a particular type of stress fracture of the tibia which is difficult to diagnose because it is an incomplete fracture involving only one cortex of the bone, and is not apparent in the radiographs until a later stage.

The author presents a very convincing argument, substantiated by radiographs, to show that all so-called "shin splints" are actually incomplete cortical fractures. The initial radiograph may be negative. Subsequent ones may show periosteal new bone formation or callus. Many of these will reveal an incomplete fracture line. Rest is the most essential part of the treatment. Occasionally a cast may have to be applied.

If the diagnosis is made early, the athlete may well be able to resume training within a few months, but when advice is neglected until late, or the condition is not recognized and sport allowed to continue, many months of disability may ensue.

Twenty-one roentgenograms; 1 photograph; 4 tables.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Variation in the Roentgenographic Density of the Os Calcis and Phalanx with Sex and Age. Harald Schraer. J. Pediat. **52:** 416–423, April 1958. (Biophysics Laboratory, Pennsylvania State University, University Park, Penna.)

Using standardized roentgenograms, the author determined the x-ray density coefficients of the left os calcis of 738 boys and 746 girls, and the middle and end sections of the second phalanx of the left fifth finger in 395 girls and 624 boys all between the ages of seven and twenty years. For the roentgenograms 8 × 10-inch no-screen film in cardboard holders was exposed at 55 kvp, the mass varying with focal film distance and the size of the object. A computing machine was used to evaluate the mas of bone in a cross-sectional slice of bone and surrounding flesh, from the roentgen image. The anatomic section evaluated is referred to as a "trace path." Results were grouped by sex in age ranges of 7 to 9, 10 to 12, 13 to 15, and 16 to 20 years.

The mean density coefficient of both bones increased significantly with age in both sexes except for the os calcis trace path of the females between age groups 13 to 15 and 16 to 20 and the phalanx center trace path of the males between age groups 7 to 9 and 10 to 12. This gradual increase with age appears to reflect classical growth patterns. In both sexes the phalanx showed higher density coefficients than the os calcis. The magnitude of the standard deviation was such that an individual set of values could not serve to designate the sex and age of the subject except in extreme cases.

Sexual dimorphism was found to exist, the phalanx density coefficients of the females being significantly greater than those of the males of the same age while except for the 7 to 9-year group, the os calcis values of the male were significantly greater than those of the females. Some of these observations may be explained by the earlier maturation of the female skeleton. The earlier closure of the epiphyses in the female and the consequent curtailment of growth appears to accompany an increase in bone mineral concentration as indicated by the higher bone density coefficients observed in the female phalanx. This does not account, however, for the higher values found in the male os calcis, and it is conceivable that a different rate of mineralization accretion occurs in different bones, influenced by hormonal and genetic factors.

An extension of these studies to cover the span of life is planned. The compilation of adequate density coefficient values based on age and sex may afford biological standards for the study of normal variations. It may also be possible to detect pathological conditions of bone, and recovery from osseous disorders which are reflected in the measurable bone sites.

Two figures; 2 tables.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

THE SPINAL CORD

Schwannoma of Spinal Cord. K. S. Bose. Indian J. Surg. **20:** 1–3, February 1958. (Medical College Hospitals, Calcutta, India)

A rare case of schwannoma of the spinal cord in a 22-year-old male is presented. The tumor was completely intradural and extramedullary and simulated an intrinsic spinal cord tumor. Although the routine roentgenogram was normal, lumbar and cisternal myelography made it possible to localize the tumor completely before surgery. Satisfactory clinical results followed operative removal of the lesion.

Two roentgenograms.

GYNECOLOGY AND OBSTETRICS

The Uterine Isthmus and its Sphincter Mechanism, a Radiographic Study. I. The Uterine Isthmus Under Normal Conditions. II. The Uterine Isthmus Under Abnormal Conditions. Abdel Fattah Youssef. Am. J. Obst. & Gynec. **75:** 1305–1332, June 1958. (Kasr-el-Aini Hospital, Cairo University, Cairo, Egypt)

Contrast media were used for the radiographic demonstration of an isthmic canal in the uterus as a distinct segment narrower than the cervical canal below and the cavity of the corpus above. There was revealed a definite limiting constriction superiorly and another inferiorly, indicating the presence of actual superior and inferior sphincters. There was no difference in appearance of the isthmus in nulliparous and parous women.

For study of the isthmus, "isthmography" was performed on 45 normal women by injection of 4 to 5 c.c. of Lipiodol through a Jarcho cannula with special rubber cones so that only 1 to 1.5 cm. of the cannula was introduced into the cervical canal. For this procedure no sedative or antispasmodic drugs should be used and at least five minutes should elapse between insertion of the cannula and the injection of the Lipiodol. In 15 women direct hysterography was performed by injection of 2 to 2.5 c.c. of Lipiodol through a fine lumbar-puncture needle directly into the uterine cavity.

The isthmus was found to be functionally independent from the corpus. The sphincteric mechanism of the isthmus was most contracted during the luteal phase of the menstrual cycle and most relaxed immediately before and during menstruation. The uterine corpus was least active in the former phase and most active in the latter. The co-ordinated activity of these two uterine segments is fundamentally important in the normal functions of fertilization, nidation, maintenance of pregnancy, and menstruation.

Forty abnormal cases were studied. It was found that the sphincteric mechanism of the isthmus was susceptible to the ovarian steroids. Administration of progestin after estrogen priming resulted in marked constriction of the isthmus. In metropathia hemorrhagica and anovular menstruation the dilatation of the isthmus was thought to be due to unopposed estrogen effect; bleeding in such cases was painless. Certain cases of habitual abortion were found to be the result of incompetence of the isthmus, either traumatic or dysfunctional. Failure of normal relaxation of the isthmus in the immediate premenstrual period and at the beginning of menstruation was noted as the basic abnormality in 12 cases of primary dysmenorrhea. The study must be done one or two days prior to the onset of menstruation as no apparent deviation from the normal could be demonstrated in the follicular or at the height of the luteal phase.

Thirty roentgenograms.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Post-Traumatic Intra-Uterine Synechiae. P. Bergman and L. Wehlin. Acta radiol. **49:** 453–463, June 1958. (Allmänna Sjukhuset, Malmö, Sweden)

The authors present a report of 11 cases of intra-uterine synechiae, or adhesions, 4 of which were verified at operation. The remaining 7 cases were not operated upon but the histories and roentgen findings agreed well with those in the morphologically verified group and the clinical examinations suggest no other explanation for the hysterographic changes.

It is probable that the incidence of intra-uterine synechiae varies with the frequency with which damage is inflicted during the puerperium or in association with abortion. In 4 of the 11 cases reported here, curettage had been done in the puerperium, and in 4 in association with abortion. Extensive uterine synechiae were seen in all 8 cases.

Patients seek advice for various symptoms. In this series of 11 patients, 5 presented themselves because of secondary sterility. Unless the adhesions have resulted in occlusion of the internal os, which can be detected by the passage of a uterine sound, the clinical diagnosis requires the help of hysterography. Typical synechiae appear roentgenologically as well defined formations bridging the uterine cavity. This bridging is best seen in films obtained perpendicularly to the synechiae, advisable in several projections. As a rule there is only slight or no deformation of the uterine cavity, although occasionally this may be marked. Synechiae may be solitary or multiple and may involve any part of the uterus. If they are situated in the cervix-isthmus region, they may lead to occlusion. In none of the present series was there tubal occlusion.

It is sometimes difficult roentgenologically to differentiate synechiae from other intra-uterine conditions, especially submucous myoma and polyps and, rarely, intra-uterine septa. A septum is always situated medially and appears as a narrow strip.

A discussion is presented of the significance of synechiae in relationship to sterility and indications for active surgical intervention.

Eleven roentgenograms; 4 photographs.

THEODORE E. KEATS, M.D.
University of Missouri

The Diagnostic Value of Disalignment of the Foetal Cranial Vault Bones in Intra-Uterine Foetal Death. A Roentgenologic Study. Ulf Borell and Ingmar Fernström. Acta radiol. **49:** 409–415, June 1958. (Karolinska Sjukhuset, Stockholm, Sweden)

The authors investigated the value of disalignment of

the fetal bones at the coronal and lambdoid sutures in the diagnosis of intra-uterine fetal death. For this purpose they reviewed roentgenograms of 1,011 pregnant women. In 969 cases the fetus was alive and in 42 fetal death had occurred. As a result of this study it is pointed out that disalignment of the bones in question observed prior to the tenth lunar month of pregnancy and in the absence of labor pains strongly suggests death of the fetus. Level differences between these bones exceeding 4 mm., observed in the tenth lunar month of pregnancy and in the absence of labor pains, are likewise suggestive of fetal death, but not disalignment of these bones observed during labor. In 29 cases of intra-uterine fetal death, where labor pains were absent, these criteria made possible a correct diagnosis in 16.

Six figures.

THEODORE E. KEATS, M.D.
University of Missouri

THE GENITOURINARY SYSTEM

Combined Pelvic Pneumoperitoneum and Pneumocystography in Roentgen Examinations of the Urinary Bladder Wall, Especially in the Search for Neoplasia. Ottavio Trucchi. Radiol. med., Milan **44:** 421–429, May 1958. (In Italian) (Istituto di Radiologia del Policlinico Umberto I, Rome, Italy)

The diagnostic insufflation of air into both peritoneum and urinary bladder, followed by body-section radiography in 35° Trendelenburg position ("stratigraphic pneumo-pelvi-peritoneo-cystography") allows excellent visualization of the urinary bladder wall. This is particularly advantageous in the detection and study of early cancer.

Eight cases of bladder tumor are presented, 6 of which were proved by surgery, and 1 at autopsy. The eighth was examined before Co^{60} irradiation and after long-term follow-up.

Nine roentgenograms; 3 diagrams.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

TECHNIC

Stereo-Micro-Lymphangiography. Bo Odén, Sven Bellman, and Bengt Fries. Brit. J. Radiol. **31:** 70–80, February 1958. (Serafimerlasarettet, Stockholm, Sweden)

Stereoscopic microradiography does not differ in principle from other stereo technics. The object is microradiographed in two directions which correspond to the view from each eye, and the enlarged microradiographs are then viewed through a stereoscope so that an optical model of the object is obtained. There is, however, one major difference in principle as compared with photographic stereo methods. In the latter the images are formed by light reflected from the surface of the object, and the structures in the stereo images normally correspond to structures on the object. With radiographic methods the images are formed by absorption in the x-ray beam and therefore false details may appear in the stereoradiograph because of a summation effect of structures which are situated at varying depths in the object. With angiographic micro methods this source of error is greatly reduced because very clear definition of even the smallest images of contrast-filled vessels can be obtained.

The authors have previously applied stereo-microradiography to investigation of blood vessels. The present report they believe to be the first account of stereo-micro-lymphangiography. The experiments were performed on rabbits and albino mice. The technic and observations are described and it is concluded that "stereoscopic methods in microlymphangiography afford better information on the form and configuration of lymphatics than does the two-dimensional procedure. Photogrammetric calculations on the basis of measurements made on stereo-micro-lymphangiograms enable the positions of different structures to be determined in depth."

Nine stereo-micro-lymphangiographs.

RICHARD P. STORRS, M.D.
Los Angeles, Calif.

RADIOTHERAPY

Malignant Melanoma. A Combined Surgical and Radiotherapeutic Approach. Robert J. Dickson. Am. J. Roentgenol. **79:** 1063–1070, June 1958. (The Johns Hopkins Hospital, Baltimore 5, Md.)

The author reviewed 234 cases of malignant melanoma, in an attempt to determine the efficacy of postoperative irradiation as advocated by the late Dr. G. E. Richards at the Toronto General Hospital. The cases reviewed were from the tumor registries of Toronto General Hospital, the Baltimore Public Health Service Hospital, and the radiotherapy department of Johns Hopkins Hospital.

Some interesting facts regarding age, sex, and body distribution and prognosis are recorded. The classification was that suggested by Sylvén (Acta radiol. **32:** 33, 1949). Stage I includes localized melanoma confined to the skin, local recurrences, and nearby deposits in the cutaneous lymphatics. Stage II comprises those cases with lymph node metastasis confined to one node station only; Stage III consists of cases with metastatic involvement of two or more groups of lymph nodes, and those with distant metastases, evidencing a generalization of the tumor process. In this series the relative frequency was as follows: Stage I, 102 cases (43.5 per cent); Stage II, 93 cases (39.3 per cent); Stage III, 39 cases (16.7 per cent). The five-year survival rates were: Stage I, 50 per cent; Stage II, 23 per cent; Stage III, 5.1 per cent.

The treatment policy at Toronto General Hospital called for wide excision of the involved sites in Stages I and II and occasionally III, along with the lymph drainage areas, and postoperative irradiation where microscopic study confirmed the presence of malignant disease. Different plans of treatment in the three hospitals and variation from the treatment policy in one permitted the accumulation of control cases. Thus, the efficacy of surgery alone and surgery and irradiation combined could be compared.

All cases were placed in one of three categories depending upon the treatment given when the diagnosis of melanoma was first made.

The following therapeutic modalities were employed, alone or in combination: wide surgical excision, local treatment, and irradiation therapy. Group I included inadequate local measures of any character. Group II comprised all patients whose sole treatment was radical

surgery, either initially or subsequent to local interference. Group III was made up of all patients who were given any form of radiation therapy.

The five-year survival rates according to the above classification were: local therapy, 19.7 per cent; wide surgery, 26.2 per cent; radiation therapy, 41.3 per cent. For the entire group of 234 cases the figure was 32 per cent.

Attention is called to many factors in this disease which are unpredictable and intangible. Superficially, comparing results in one series of cases with another may seem valid; whereas in reality this is far from true. The overall survival rate of 32 per cent is comparable to the best figures published in a small selection from the voluminous literature on this subject.

The author is quite fair in stating that the findings in this series lend force to the suggestion that palliative radiation therapy tends to improve the prognosis in this condition. A five-year survival rate of 41 per cent in a series of 121 cases treated by surgery and postoperative irradiation or by palliative irradiation supports this contention. The findings in the series reviewed justify the opinion that postoperative irradiation in association with excisional surgery is an adequate alternative to ablative and deforming operation for malignant melanoma.

Eight tables of a statistical nature are included.

H. C. JONES, M.D.
Grand Rapids, Mich.

Lesions of the Salivary Glands. D. G. McEachen, D. F. Moore, E. M. Nanson, and T. A. Watson. Surg., Gynec. & Obst. **106:** 655–666, June 1958. (University of Saskatchewan, Saskatoon, Canada)

One hundred and fifty-five cases of salivary gland lesions seen in the Saskatoon Cancer Clinic from 1932 to 1956 are reviewed. One hundred and twenty-nine were neoplasms, of which 79 were benign mixed tumors. In general the treatment was surgery plus postoperative irradiation. Benign mixed salivary tumors had an overall recurrence rate of 6 per cent. Patients with malignant tumors had an overall five-year survival rate of 65 per cent.

The methods of radiation therapy for malignant salivary tumors are similar to those described for benign mixed salivary tumors except that the dosage is higher, the treatment field larger, and the duration of the treatment somewhat longer. For benign "only one course of treatment is given and the dosage is uninfluenced by the type of surgery done. Usually external irradiation is prescribed using a single field of a size varying from 5 by 5 centimeters to 10 by 10 centimeters depending on the extent of the tumor. A common field is 6 by 8 centimeters. With 200 to 400 kilovolt x-rays, the dosage varies from 4,500 to 5,000 roentgens in about twenty days to 5,500 to 6,000 roentgens in thirty-two days, the actual dose depending on the size of the field used. With radioactive cobalt telecurietherapy the dosage is approximately 10 per cent higher. Treatments are equal and daily. Usually the skin reaction does not progress beyond a brisk erythema. A mucositis of the pharynx is produced, with loss of taste, dryness of the mouth, and sometimes dysphagia. All of these symptoms are transitory. There has been no necrosis or late reaction.

"In some cases, when a tumor of the parotid is confined to the flat preauricular area and does not appear to extend deeply, posterior to the ascending ramus of the mandible, a single plane radium implant is performed, either at the time of the excision or ten days later, the former being preferable. There is no interference with the healing of the wound. The area implanted is approximately 6 by 6 centimeters and a dose of 6,000 roentgens in 170 to 200 hours at 1/2 centimeter from the plane is prescribed. There is no reaction to this treatment except a brisk erythema of the skin which sometimes proceeds to moist desquamation."

The authors believe that the best results in treating salivary tumors are obtained with adequate surgery plus adequate irradiation. Radiation is always used as an adjunct to surgery.

Fourteen tables.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

End-Results in Carcinoma of the Oral Cavity. A Study Based upon Six Hundred Seventy-Nine Cases over a Fifteen-Year Period. Samuel L. Perzik, Eugene J. Joergenson, Richard P. Carter, and Paul H. Deeb. Arch. Surg. **76:** 677–681, May 1958. (S. L. P., 300 S. Beverly Dr., Beverly Hills, Calif.)

The location and the five-year results for 679 carcinomas of the oral cavity are reported.

Site	No. of Cases	Five-Year survival
Lip	152	43%
Tongue (including floor of mouth)	278	13%
Tonsil	105	2%
Lower gum	44	5%
Upper gum	16	20%
Buccal mucosa	35	30%
Soft palate	31	7%
Hard palate	18	18%

The relatively low five-year cure rates reported are partially on the basis of the stage of the tumor when first seen. Almost one-third of the intraoral cancers (excluding those of the lip) were so far advanced on admission that it was not possible to undertake definitive curative treatment. When the untreated cases are excluded, the five-year rate is 22 per cent for cancer of the tongue and 17 per cent for all intra-oral cancers (excluding lip).

The problem of cancer of the tongue was analyzed in detail to determine the favorable or unfavorable factors. The overall five-year cure rate for females with cancer of the tongue is 24 per cent as against 13 per cent for the entire group. As would be expected, the size of the lesion was important. In over 62 per cent of the series the primary lesion measured over 3 cm. in diameter, and in this group the five-year cure rate was 7 per cent, about half that for the group as a whole. With the primary lesion in the base of the tongue (20 per cent incidence), the cure rate was zero. The presence or absence of metastatic lymph nodes was also an influencing factor. Syphilis was present in 22 per cent of the patients with cancer of the tongue, and in this group the cure rate was 7 per cent.

Therapy consisted of surgery or irradiation, or both. The two modalities are not competitive. Treatment must be individualized as to type and sequence. It must be complete and all-encompassing at the time of initial management.

Eight tables.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

Results of Irradiation in 770 Cases of Bronchial Carcinoma. Werner Hellriegel. Strahlentherapie **106:** 112–122, May 1958. (In German) (Universitäts-Röntgeninstitut Frankfurt a.M., Germany).

The author reports the results of irradiation in 770 advanced cancers of the lung treated between 1945 and 1955. The ratio between males and females in this series was 7.6 to 1. Most of the patients were in the age group between fifty-six and sixty. In younger women—below forty—the incidence of these neoplasms was high; they constituted 50 per cent of all tumors in that group.

The sedimentation rate was high in 70 per cent of the cases. The vital capacity of the lungs was diminished in 71 per cent, and over 44 per cent showed tumor cells in the sputum or pleural exudate. In 32.2 per cent the diagnosis was confirmed by biopsy and roentgen examination, in 30.1 per cent by cytology, surgery, and roentgenograms, and in 37.7 per cent the diagnosis was made by the roentgen examination alone.

Among 250 cases, there were 58 per cent squamous-cell cancers, 40.4 per cent undifferentiated carcinomas, and 1.6 per cent adenocarcinomas. The tumor occurred in the right lung oftener than in the left. The upper lobes were more frequently involved.

Only 16.7 per cent of the patients survived one year, and 2.8 per cent five years. Of 75 patients who received a combination of surgery and radiation therapy, 37 per cent were alive after one year and 16 per cent after five years.

The method of irradiation consisted in the use of pendulum therapy and stationary fields. With pendulum therapy, 8 per cent of the patients survived five years; with stationary fields, only 2.5 per cent. The average survival with stationary fields was 5.3 months, with pendulum therapy 10.2 months. With stationary fields the average tumor dose was 4,000 r, while with pendulum therapy the average dose was 9,000 r.

Adenocarcinoma of the lungs has a very poor prognosis. None of the patients survived one year. Poor results were also obtained in the undifferentiated lung tumors. None of the patients survived five years and only 2.4 per cent three years.

The author states that, in spite of diligent efforts to improve our methods, the end-results of radiation treatment of lung cancer are still very discouraging.

One graph; 16 tables.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Radiation Therapy of Lung Tumors. Albert Kohler. Strahlentherapie **106:** 106–111, May 1958. (In German) (Röntgeninstitut bei der Chirurgischen Klinik der Universität München, Germany)

The author believes that squamous-cell cancers of the lung grow slowly and are most suitable for surgery. The small-cell, undifferentiated cancers grow rapidly, they are usually not amenable to surgery, but seem to respond well to radiation therapy. The author calls attention to the poor co-operation between surgeons and radiologists. Very frequently surgeons discharge their patients without any plans for postoperative radiation therapy, this being ordered only when the symptoms get worse. The unnecessary delay is often responsible for poor results.

At the University of Munich 410 cases were treated from 1938 to 1955, and 367 cases were evaluated for statistical purposes. Pendulum therapy was used, at 60 or 50 cm. distance. The average tumor dose ranged from 5,500 to 6,000 r.

Up to 1952, 6.8 per cent of the patients were alive after five years. Since that year, the three-year survival had fallen to 1.5 per cent. Due to the increase in surgical therapy, only far advanced cases are now reaching the Department of Radiation Therapy, accounting for the poor results as compared with previous years.

The author believes that palliative treatments should be given with relatively low dosages in order to avoid a high mortality within the first three months. He advocates the use of preoperative irradiation and hopes to improve results by the combined method. The conclusion is reached that cancer of the lung is curable in only a very small percentage of cases with radiation therapy alone.

Two figures; 1 table.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Radiation Therapy for Recurrent Carcinoma in the Bronchial Stump. Harry J. Pinsky and George L. Emerson. J. Thoracic Surg. **35:** 683–688, May 1958. (H. J. P., 2455 Elka Ave., Mountain View, Calif.)

Habein, McDonald, and Clagett, in 1956, recorded 18 cases of bronchogenic cancer, with recurrence in the bronchial stump, in several of which irradiation was given (J. Thoracic Surg. **31:** 703, 1956). The present authors have recently seen 4 cases with such recurrence, 1 of which is reported. The marked palliation achieved in this case, with surgery and repeated courses of radiotherapy, has encouraged them to utilize a similar plan in the remaining cases. It is too early to evaluate the results in these 3.

The patient was a 57-year-old man, first seen in April 1952, with a history of chronic respiratory infection dating back to 1945. He had been a heavy cigarette smoker for twenty-five years. Roentgenograms and fluoroscopy of the chest disclosed an enlargement of the right root and partial atelectasis of the right lower lobe. Bronchoscopy revealed a large mass in the right main bronchus just below the carina. The histologic diagnosis on tissue removed at bronchoscopy was epidermoid carcinoma. A right pneumonectomy was performed on April 25. The patient gained weight, had less dyspnea, and returned to work. In May 1953, weight loss, cough, and hemoptysis recurred. Bronchoscopy in August 1953 revealed recurrent tumor in the right main bronchial stump, with tumor partially occluding the left main bronchus as well. In an effort to clear the airway, the bronchoscopist removed as much tumor as possible. A course of roentgen therapy was then given with the carina as the center of rotation, a 10 × 10 cm. port, and a focal-axis distance of 100 cm. One-million-volt radiation was employed at 3 ma, with a half-value layer of 9.0 mm. copper. Over a period of thirty-eight days, a tumor dose of 5,200 r was delivered in twenty-six treatments. The patient tolerated the treatment well, showing progressive improvement and experiencing only minimal reddening of the skin over the sternum. He did very well thereafter, complaining only of slight dyspnea, until February 1955, when he again raised blood-streaked mucus. On Feb. 18, 1955, bronchoscopy again revealed recurrent tumor in the bronchial stump on the right, partially occluding the left main bronchus. The bronchoscopist again removed as much tumor as feasible and a second course of irradiation was given (5,000 r to the carina, with the factors used previously),

Cough and dyspnea diminished and the patient was able to continue work throughout treatment. In June 1956, cough returned along with hemoptysis and dyspnea, and again the bronchoscopist cleaned out as much tumor as technically possible and obtained pathologic proof of recurrent epidermoid carcinoma. A third course of radiotherapy was given, 5,000 r again being delivered to the tumor, with the patient continuing at his job with some exertional dyspnea and cough. On Oct. 21, 1956, four years and a half following the original surgery, an upper respiratory tract infection developed and death occurred with a massive pulmonary hemorrhage.

At necropsy, an area of necrosis, measuring 4 × 5 cm., was found in the tracheobronchial tree at the location where recurrent tumor had been seen at bronchoscopy prior to irradiation. This was thought to represent the source of terminal hemorrhage. No definite evidence of residual tumor cells was found on detailed pathological investigation of sections through the area of necrosis or elsewhere. A moderate degree of radiation fibrosis was present in the remaining lung, as well as some pleural fibrosis.

The authors' experience shows that, in selected cases, a second course of radiation therapy can be tolerated. They recommend further investigations in situations other than bronchial stump recurrence as to the potential value of repeated irradiation in the long-term control of bronchogenic carcinoma.

Four roentgenograms; 6 photomicrographs.

Dosage Control by Direct Measurement in the Radium Treatment of Uterine Carcinoma. W. G. Evans and D. V. Mabbs. J. Fac. Radiologists **9**: 66–67, April 1958. (Royal Berkshire Hospital, Reading, England)

In the technics used for the treatment of cancer of the corpus or cervix uteri, dosage to the primary growth can be calculated with sufficient accuracy. Calculation of the rectal or parametrial dose is made more uncertain by possible asymmetry of radium sources or pathological displacement of the uterine body or vaginal vault. Since the rectal or vesical dose is often the limiting factor in treatment, it is important to know these doses and more realistic to make a direct measurement in each case than to attempt to calculate them. The treatment technics used at the Royal Berkshire Hospital (Reading, England) are described.

A record of any rectal or vesical reaction was kept for each of 65 consecutive cases receiving gynecological radium therapy during 1954–1956. Eight patients who either received a rectal dose in excess of 5,000 r, or this dose in less than seventy-two hours, had rectal tenesmus of some severity. In no instance was the vesical reaction more severe than the rectal so that it appears that a safe rectal dose ensures a safe bladder dose in most cases if the anterior fornix is carefully packed. The authors believe that, at the cost of very little time, rectal overdosage may be avoided and straightforward dosage measurements can be made in the pelvis to guide later supplementary x-ray therapy.

Two roentgenograms; 1 graph; 1 table.

On Localization of the Focus in Pendulum Radiotherapy of Gynecological Tumors. Kuno Knopp. Strahlentherapie **105**: 315–317, February 1958. (Universitäts-Frauenklinik Würzburg, Germany)

The author describes a device which permits the exact localization of the focus in the parametrium or uterus for pendulum irradiation. This consists of a compass, one shank of which contains a guide for the transvaginally palpating index finger. The other shank bears a grease pencil which stands in exact opposition to the fingertip of the examiner and serves to mark the beam entrance on the patient's skin. A caliper scale indicates the depth of the tumor simultaneously.

A horizontal and vertical water level are also attached to this instrument.

Two photographs. GERHART S. SCHWARZ, M.D.
New York, N. Y.

Rotational X-ray Therapy Planned to Complement Radium Treatment of Carcinoma of the Cervix Uteri. Gertrude Goldscheider and Babette E. Stern. Brit. J. Radiol. **31**: 88–92, February 1958. (Marie Curie Hospital, London, N.W. 3, England)

The authors supplement the radium dose in carcinoma of the cervix with moving field deep roentgen therapy, at 250 kv, with Thoraeus I filter, h.v.l. 2.5 mm. of copper. The radius of rotation is 60 cm.

When the patient's condition permits, treatment is usually started with radium (modified Stockholm technic) and arc therapy follows the second radium application. The treatment is planned to raise the dose to 4,500 r (X) to the whole pelvic cavity and avoid overdosage of the femoral neck, bladder, rectum, and volumes of tissue fully treated with radium.

Details of the method of planning the therapy are given (See also abstract of paper by Snelling and Stern, p. 629). The authors feel that the immediate response of their patients to this procedure has been gratifying, though the ultimate value will be assessable only after lapse of more time.

Five figures; 1 table. RICHARD P. STORRS, M.D.
Los Angeles, Calif.

Carcinoma of Bladder with Cutaneous Recurrence Following Partial Cystectomy: Ten Year Cure by External Irradiation. C. M. Burgess, W. S. Strode, and P. S. Arthur. J. Urol. **79**: 961–963, June 1958. (1020 Kapiolani St., Honolulu, Hawaii)

A primary anaplastic carcinoma of the dome of the bladder which had infiltrated the bladder wall was excised widely through a suprapubic incision. Metastatic disease occurred seven months later in the skin incision. The tissue was identical with the primary tumor. A block dissection of the metastatic mass and surrounding tissue was done but less than a month later a second mass developed in the incision. Following treatment with 200-kvp x-rays, 200 r daily (in air) to a total of 2,000 r to each of four pelvic ports there was complete regression of the tumor and nine and a half years later there was no evidence of recurrence or metastases.

Two photomicrographs.

ROBERT S. ORMOND, M.D.
The Henry Ford Hospital

Hemangioma of the Bladder. Daniel S. Liang. J. Urol. **79**: 956–960, June 1958. (155 Angell St., Providence 6, R. I.)

Two cases of hemangioma of the bladder treated with 2,500 r in air in ten divided doses are presented. Complete disappearance of the tumors occurred with no untoward side-effects.

Intravenous pyelograms in each case revealed a filling defect in the bladder. There was unilateral obstructive hydronephrosis in one case, and gross hematuria in

the other. The hemangioma was visualized through the cystoscope as a bluish-brown, broad-based tumor. Follow-up cystoscopy after therapy revealed complete resolution of the process.

Two roentgenograms; 2 photomicrographs.

ROBERT S. ORMOND, M.D.
The Henry Ford Hospital

Arc Therapy with 250 Kv X Rays: A Symposium. I. Basic Physical Problems. Frank T. Farmer. Brit. J. Radiol. **31:** 285–290, June 1958. (Royal Victoria Infirmary, Newcastle upon Tyne, England)

As early as 1906 Kohl described a form of apparatus which would move about a patient in a circular arc, directing its beam to a fixed point within the body. It is known that arc therapy, while delivering an adequate tumor dose, spares the skin as compared to fixed-port therapy. The integral dose, however, must also be considered. This article discusses the relationship between tumor dose, maximum skin dose, and integral dose.

An asymmetric pelvic tumor was chosen for demonstration of this relationship. With rotation therapy (360°), the skin dose was held to a minimum, while integral dose was found to be quite high. Integral dose was reduced with the use of three fixed fields, at the expense of skin dose, which was increased almost twofold. By use of three fixed fields with applicators, integral dose was still further reduced, while skin dose continued to increase. The four-fixed-field technic with compression was found to decrease integral dose to the lowest figure, with an acceptable skin dose.

The author also discusses the possibility of using smaller arcs in an effort to reduce integral dose and approach the figures obtained in fixed-field methods. Although arc therapy clearly has its advantages in its lower skin dose, it can be stated, in general, that volume dose will be greater than in a well planned fixed-field treatment technic.

Eight figures; 1 table.

EARL BROWN, JR., M.D.
Indiana University Medical Center

Arc Therapy with 250 Kv X Rays: A Symposium. II. The Effects of Some Variables on Arc Therapy Dosage Distributions. J. F. Fowler. Brit. J. Radiol. **31:** 290–293, June 1958. (King's College Hospital, London, S. E. 5, England)

The author discusses the effect of quality of radiation, bone absorption, change in position of the treated region, and presence of lung on arc therapy dosage distributions.

It is concluded that radiation of higher quality gives a definite though rather small advantage in both skin and integral dose.

For determination of the effect of bone absorption, measurements were made in two transverse planes in an abdominal phantom, 1 and 3 cm. above the symphysis pubis, with and without the presence of wax-filled bone. Some reduction in maximum dose was obtained with bone, a little greater in the lower of the two planes. With a slight increase in hardness of the radiation, the reduction due to bone absorption was markedly less. The effect of the thoracic cage was also studied and here again it was found that with lower quality radiation larger reduction factors were obtained.

The author also demonstrates by use of graphs the effect on maximum dose of shifting of the center of rotation in the anteroposterior and lateral directions.

By the use of both air and water phantoms, it was shown that there is a considerable increase in maximum dose due to the presence of lung.

Seven figures; 1 table.

EARL BROWN, JR., M.D.
Indiana University Medical Center

Arc Therapy with 250 Kv X Rays: A Symposium. III. Five Years' Experience of Arc Therapy. Oliver Chance. Brit. J. Radiol. **31:** 293–298, June 1958. (St. Luke's Hospital, Dublin, Ireland)

Five years ago (1953) a Mueller 200-kv rotation unit in which the tube traveled 330° on the arc of a circle with a radius of 50 cm. was installed in St. Luke's Hospital, Dublin. While an overall period of five years is not long enough to permit the evaluation of any form of treatment on a statistical basis, it is sufficient for arriving at an opinion as to the merits of arc therapy.

The problem of dosage was the first hurdle. When a source of radiation rotates around a point in a noncylindrical mass of varying density, such as the human body, changes occur constantly during each rotation, all of which affect dosage. These involve the focal-skin distance, skin-field size, surface-tumor distance, the time which different regions remain in the beam, and tissue density.

Some method of dose calculation is necessary which is reasonably accurate and yet feasible for use in a busy therapy department. O'Connor (Brit. J. Radiol. **27:** 453, 1954) developed a calculator by which the dose at any point in the irradiated body section can be determined rapidly. It is based on isodose curves calculated for stationary fields and consists of a circular protractor on which an arm is moved through the proposed arc of treatment while at the same time, by means of a sliding adjustment, the dose received at any point is recorded, the total dose being summated. Direct measurements with ionization chambers placed in the body have confirmed the practical value of this calculator.

The chief indications for arc therapy are (1) carcinoma of the lower two-thirds of the esophagus, where it is possible to obtain a distribution which permits a high tumor dose while keeping the skin dose at a safe level; (2) for supplementary therapy to the parametria in cancer of the cervix treated with radium; (3) pituitary tumors. Accurate location of the lesion is of prime importance because small fields are used and the source of radiation is in motion. An error of 1 cm. in centering can produce considerable error in dosage.

In *carcinoma of the thoracic esophagus* the field at the center of rotation is 15 × 4 cm. Rotation is through an arc of 330°, avoiding the segment over the spinal cord. A tumor dose of 5,500 to 6,000 r is given in five to six weeks. The dose to the cord is never more than 2,000 r and the skin dose varies between 1,600 and 2,250 r. Patients tolerate the treatment well. A moist reaction occasionally develops, but this is limited to a small skin area over the sternum, where the contour is flat. Twenty-eight patients received therapy, 26 to conclusion, and 18 showed improvement in swallowing. The average survival period was 8.5 months. The patients tolerated treatment better than when fixed fields are used and therefore more received a full course of treatment, resulting in better palliation.

For *carcinoma of the cervix*, the dose distribution of the radium is first calculated and each side of the pelvis is treated through an arc of 210° leaving a gap of 40° over the head and neck of the femur. The average combined dose to the parametria is 5,000 r. The skin dose is

never more than 2,500 r. A very small displacement of the point of rotation can produce excessive dosage at point "A" or in the head of the femur. One patient sustained a fracture of the femoral neck as a result of an outward displacement of 1 cm. in the center of rotation. The results varied little from those obtained with fixed-field methods but the impression was that patients tolerate treatment better.

For *pituitary tumors*, 360° rotation was used. This gives a skin dose 30 to 50 per cent of the tumor dose. The plane of rotation is along the fronto-occipital axis to avoid irradiation of the orbits. A maximum tumor dose of 3,500 r is delivered in five weeks. Epilation, if it occurs, is not severe, and none of the author's patients had permanent baldness. Results were no better than those obtained with other methods but the treatment is easier.

The author feels that from the point of view of cure arc therapy has no real advantage, but that it does perhaps produce a slightly higher degree of palliation with less discomfort to the patient.

Four figures.

PAUL M. INLOW, M.D.
Indiana University Medical Center

Arc Therapy with 250 Kv X Rays: A Symposium. IV. The Treatment of Carcinoma of the Cervix by a Combination of Intra-cavitary Radium and Arc Therapy. Margaret D. Snelling and Babette E. Stern. Brit. J. Radiol. **31**: 298–306, June 1958. (M. D. S., Middlesex Hospital, London, W. 1, England)

The work upon which this paper is based was done at the Marie Curie Hospital (London). Arc therapy, on the whole, offered no advantage over conventional methods for treating large volumes, since this implies the use of large fields and arcs through the wider diameters of the patient and often through bone. The technic is of value in treating the parametria, since small arcs can be used and much the same area of the skin is traversed as would be selected for fixed fields. The real advantage is in treating the obese patient where the dose in the parametrium can be increased by 3,000 to 4,000 rads (250 kv, h.v.l. 2.5 mm. Cu) in four weeks without approaching the tolerance level of the skin. This is a dose rate which cannot be easily achieved with stationary small fields using this quality of irradiation.

The radius of rotation is 60 cm., with a field length of 14.4 cm. at the center of rotation. The arc of rotation is 70° arranged so that in the extreme medial position the edge of the beam passes through the skin about 1 cm. lateral to the midline on the side to be treated. A slightly larger gap is left posteriorly to avoid overirradiation of the rectum. Anterior and posterior ports are utilized on both sides. The dose received per 100 r in air at the center of rotation is worked out for points A and B.

Arc therapy is begun after the second or third insertion of radium and is planned individually for each patient. The radium technic is based on the original Stockholm method for a dose at point A of 5,000 to 6,500 rads. The dose at point B is between 1,000 and 3,000 rads. By arc therapy it is planned to bring the level of dosage at point B to 4,300 rems without adding unduly to the dosage received in the volume already adequately treated with radium.

The disadvantage of arc therapy as described is the time spent in its planning and in setting up the patient and actually delivering the dose each day. This is reduced by having a team of experts, but the treatment time itself must be long and lasts for perhaps twenty minutes for each field, which is a disadvantage in a busy department. It is felt, however, that in the absence of supervoltage the time and effort are worthwhile.

Eleven figures, including 1 roentgenogram.

PAUL M. INLOW, M.D.
Indiana University Medical Center

Irradiation of the Entire Skin Surface of the Body with Long Wave Roentgen Rays. G. L. Sannazzari. Radiol. med., Milan **44**: 564–590, June 1958. (In Italian) (Istituto di Radiologia dell'Università di Torino, Italy)

For roentgen therapy of low penetration, tubes with beryllium windows (which allow the exit of long-wave roentgen rays) and large focal spots (which permit the use of 25 ma currents) are used. The author employed the Dermopan, made in Germany by Siemens, but similar models are carried by other manufacturers. The main advantages are (1) the steep fall-off, comparable to but not quite as abrupt as that in contact irradiation; (2) half-value layers with significant differences even at the millimeter level, wishfully labeled "cutaneous stratitherapy," (3) short irradiation times, because of the high intensity beam, and (4) a safety device which, in the absence of a filter, shuts off any current above 10 kvp.

A phantom was constructed from Plexiglass rectangles (100 sq. cm. surface, thicknesses from 1 to 10 mm.) stacked with interposed petrolatum. The Dermopan was set up for the following technics: h.v.l. of 0.35 mm. cellon (10 kvp without filter); h.v.l. of 0.2 mm. Al (29 kvp with 0.3 mm. Al filter); h.v.l. of 0.5 mm. Al (43 kvp with 0.6 mm. Al filter); h.v.l. of 0.9 mm. Al (50 kvp with 1.0 mm. Al filter). The intensity of the tube current remained constant at 25 ma. Measurements—with a Siemens ionization chamber connected to a universal dosimeter of the same make—were made to determine both the fall-off, from millimeter to millimeter, and the distribution over the entire field. The focal distances used were 1, 1.5, and 2 meters, for h.v.l. of 0.9, 0.5, and 0.2 mm. Al. The fall-off was also measured for tube-skin distances of 20 and 30 cm., to evaluate the degree of "hardening" of the beam with increasing T.S.D.

The centerpoint of a man of average height (1.70 m.) is about 12 cm. below the umbilicus. When the tube is placed at 2 meters T.S.D. perpendicularly above the centerpoint, only with h.v.l. of 0.9 mm. Al can acceptable distribution be obtained (70 per cent at the two extremes of head and toe; 100 per cent over the palms if the hands are in anatomical position). Actually, a very satisfactory distribution for total body skin irradiation requires four "portals" at 1.0 m. T.S.D.: the central ray is directed successively over four points, two anterior and two posterior, equidistant from the centerpoint, *e.g.*, at 60 cm. for 0.9 mm. Al h.v.l., at 55 cm. for 0.5 mm. Al and at 50 cm. for 0.2 mm. Al h.v.l.

The fall-off in depth with any of these three half-value layers is sufficiently steep to permit the use of high dosages without the danger of radiation sickness or of anemia, two of the limiting factors in teleroentgentherapy when medium or short wavelengths are employed. No such occurrences are ever encountered in low-penetration roentgen therapy.

The quality of this radiation should be adjusted to the condition treated: 0.2 mm. Al h.v.l. is employed

for "benign" conditions (neurodermatitis, eczema, erythroderma, various dermatoses), while 0.5 and 0.9 mm. Al h.v.l.'s are reserved for "malignant" problems (mycosis fungoides, cutaneous reticulosis, cutaneous metastases, cutaneous Hodgkin's disease).

This paper does not include clinical observations.

Twenty-four graphs; 3 drawings; 3 tables.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

The Roentgen and the Rad and Their Use in Radiology. H. E. Johns. J. Canad. A. Radiologists **9:** 36–39, June 1958. (University of Toronto, Toronto, Ont., Canada)

Since the advent of higher energy x-ray machines and radioactive isotopes, the necessity for uniform dosimetry has become more acute. The Internationall Congress on Radiological Units (I.C.R.U.) introduced the absorbed unit, the "rad" in 1953. At the I.C.R.U. meeting in Geneva, in 1956, the commission recommended that the roentgen be a unit of exposure, and the rad be the unit of absorbed dose. Their formal definition of the roentgen remains the same. The definition of absorbed dose of any ionizing radiation is the energy imparted to matter by ionizing particles per unit mass of irradiated material at the place of interest. One rad is 100 ergs/gm.

When it comes to expressing absorbed dose from a beta emitting radioactive material, in terms of the concentration in millicuries/gm. present at the point of interest, one merely multiplies the number of disintegrations per second by the mean energy of the disintegration to obtain the energy absorbed in ergs/gm. If this is divided by 100, we obtain the dose in rads. The rep, previously used for this type of dose estimation, is no longer recommended.

This article contains tables showing conversion factors from roentgens to rads. For a complete report on conversion factors, reference is made to *Handbook 62*, National Bureau of Standards, Washington, D. C.

One graph; 2 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

RADIOISOTOPES

Use of Radioisotopes in the Diagnosis of Anemia. Philip C. Johnson, Robert M. Bird, and William L. Hughes. Arch. Int. Med. **100:** 544–548, October 1957. (University of Oklahoma School of Medicine, Oklahoma City 4, Okla.)

While there is great enthusiasm for the use of radioactive isotopes as investigative tools in the study of hematologic disorders, their application to clinical diagnosis has not been so readily accepted. At present the general consensus is that vitamin B_{12} labeled with cobalt 60, erythrocytes labeled with chromium 51, and iron salts labeled with iron 59 should make an important contribution to the clinical classification of the anemias. The authors have reviewed the experience of the Radioisotope Service, University of Oklahoma School of Medicine, to determine whether these isotopic technics furnish information which is unique or supply data more accurate and more readily measurable than that obtained with conventional diagnostic procedures. Investigations employing iron 59 for clinical testing by measuring plasma-iron disappearance rates, erythrocyte-iron reappearance times, and intestinal absorption of iron failed to yield information which cannot be obtained more readily by nonisotopic methods, and the article is largely devoted to a discussion of the studies with cobalt 60-vitamin B_{12} and chromium 51-labeled erythrocytes.

Intestinal absorption of cobalt 60-vitamin B_{12} can be measured by determining the percentage of radioactivity excreted in the stool and urine or by the percentage of radioactivity present in the liver area. Each procedure permits identification of intrinsic-factor deficiency, which is not readily possible by other means. Vagaries of stool and urine collection are such as to make the scintillation count of the liver more practical. This technic has a high degree of accuracy in differentiating pernicious anemia from other anemias and is not influenced by previous vitamin B_{12} therapy.

Homologous erythrocytes can be labeled with radioactive chromium 51 and reinjected. Determination of the percentage of radioactivity remaining on the eighth day gives information of clinical value in approximately half of the patients in whom the possibility of a hemolytic anemia exists.

One chart; 3 tables.

Topical Beta Ray Therapy for Superficial Skin Carcinomata and Keratoses. Merall Roth and James N. Castle. Am. J. Roentgenol. **79:** 927–960, June 1958. (M. R., 14 Via Cheparro Drive, San Rafael, Calif.)

The authors have modified Low-Beer's original technic of applying P^{32} to multiple areas of superficial skin carcinomata (Am. J. Roentgenol. **58:** 4, 1947. Abst. in Radiology **50:** 722, 1948). To improve the distribution of the radioactive material they suggest two modifications of the procedure. For the first, known as "edge immersion" method, a blotting paper patch is cut to fit the size of the lesion and is then immersed in a measured drop of solution of known activity sufficient to saturate it by capillarity. It is then dried, autographed, and taped to the skin. For the second, applicable to larger areas, a wetting agent is added to the solution to facilitate an even spread of activity. The activated blotting paper is glued to the inside of a lead foil and taped to the skin.

Clinical observations were made on 12 patients on whom 91 patches were applied. The results are presented with clear cut graphs and excellent photographs.

Superficial skin cancer and keratoses received to 4,000 μc hr./cm.^{2} with air-backed patches. This was reduced to 2,500 μc hr./cm.^{2} with lead backing, due to 60 per cent back-scatter from the lead. As one might expect, large patches tended to produce a greater maximal reaction but the acute reaction, recovery, and late changes were nearly the same for large ports as for small ones. Treatment time varied from eleven to forty-nine hours. Peak reactions occurred on the twelfth to the eighteenth day. Healing occured by the ninth week. About 60 per cent showed pink atrophy as the initial late change.

This method has a decided advantage over roentgen therapy because of the rapid fall off in dose which minimizes the injury to the deeper layers of the skin and structures immediately beneath it. Since beta rays of

P^{32} have a maximum range of 8 mm. in tissue, new skin can grow from sweat glands and deep hair follicles beyond the effective range of the beta particles. Bone marrow is not depressed and there are no significant systemic reactions. This type of treatment, however, is limited to lesions which are about 1 mm. in thickness; thick crusts should be removed if possible.

Eleven radioautographs; 64 photographs; 5 graphs; 14 tables.

ROBERT H. LEAMING, M.D.
Memorial Center, New York

The Treatment of Lung Cancer (Primary and Metastatic) by Radioactive Phosphorus Administered Intravenously, Intra-Arterially and Intracardially. Irving M. Ariel. Am. J. Roentgenol. **79:** 961–980, June 1958. (139 East 36th St., New York, N. Y.)

Because of the long hospital stay for the palliative treatment of lung carcinoma, either primary or secondary, and the transient palliation obtained when radioactive material has been injected into lesions found to be inoperable, the author investigated a method of affording such patients the benefits of radiation without subjecting them to prolonged external irradiation or thoracotomy.

Radiophosphorus was administered intravenously in the form of radiophosphate as sterile isotonic sodium phosphate solution diluted with normal saline. Approximately 1 c.c. was made to contain 1 mc of phosphorus on the day of administration and an average single dose of 5 mc of P^{32} was given. This was usually repeated in a week. In some instances a single dose of 10 mc was given. Attempts to enhance the concentration of the isotope were made by injecting it intra-arterially and directly into the heart and by giving a preliminary course of nitrogen mustard. Determinations of the quantity of P^{32} in the lungs were made by a scintillation counter. Thorough checks of the blood count were made before and after the isotope therapy.

The effects of treatment were determined in primary as well as secondary lung carcinoma. Data on 51 patients are included. The author concludes that P^{32} in an average dose of 10 mc afforded symptomatic relief in a significant number of patients but offered no significant prolongation of life.

Primary lung tumors and tumors metastatic from primary breast carcinoma responded best to intravenous P^{32}. There were no serious untoward reactions. Attempts to enhance the concentration of the isotope in lung tumors by administering the isotope intracardially, intra-arterially, or subsequent to a course of nitrogen mustard were unsuccessful.

Thirteen tables.

ROBERT H. LEAMING, M.D.
Memorial Center, New York

Interstitial Implantation in the Treatment of Primary Bronchogenic Carcinoma. Ulrich K. Henschke. Am. J. Roentgenol. **79:** 981–987, June 1958. (Memorial Center, New York, N. Y.)

In a review of the literature the author points out that about one-third of all patients with primary bronchogenic carcinoma are explored with the intent of carrying out a resection. Nearly half of these patients are inoperable at the time of surgery. To compensate for this unfortunate situation interstitial implantation of a radioactive source at thoracotomy is recommended. This is not a hazardous procedure either to the patient or hospital personnel and no serious complications have been encountered. A much higher tumor dose can be delivered and in many cases the implantation can substitute for a postoperative course of radiation therapy.

The results in a series of 119 patients in whom this procedure was followed at Memorial Hospital (New York) between 1941 and 1955 are reported. No resection was performed in these cases, but in many of them supplemental external radiation was employed.

Significant results were attained in superior sulcus tumors, for one of which the only five-year survival in this group of 119 patients was obtained.

Unloaded hollow needles, 15 cm. long, are first placed in and around the tumor and the implanted volume is determined by measuring the separation of the needles and their outside length. The exact number of sources required for the desired tumor dose is then calculated and, with a special instrument attached to each needle in turn, these are introduced. With this technic implantation is more accurate, tumor dose can be more precise, a number of sources can be introduced through the same needle, and radiation to personnel is reduced.

Many artificial radioisotopes have been evaluated. Iridium 192 with its long half-life, smaller diameter, reduced exposure to hospital personnel, and relatively low cost, seems to be the radioisotope of choice.

Six figures, including 2 roentgenograms; 4 tables.

ROBERT H. LEAMING, M.D.
Memorial Center, New York

The Endobronchial Irradiation of Bronchial Carcinoma. Hans-Jürgen Brandt and Werner Schlungbaum. Strahlentherapie **105:** 207–217, February 1958. (Strahleninstitut der Freien Universität Berlin am Städt. Krankenhaus Westend, Germany)

For radiotherapy of bronchial carcinoma, the authors introduce a chain of cobalt pearls into the affected bronchus, through a special slender bronchoscope. The procedure is carried out under general anesthesia with a closed-circuit breathing bag. Once the pearls are affixed to the tumor by means of guiding wires, the bronchoscope is removed. The maximum duration of application is four hours per session, which delivers a contact dose of 4,000 r. More than 50 patients have been treated in this manner.

The following indications are mentioned: (1) inoperability; (2) intolerance to external radiation; (3) predominantly endobronchial tumors with stenosis of the larger bronchial branches; (4) postoperative bronchial stumps; (5) superficial spreading tumors (within bronchi or the trachea).

Six case reports are presented.

Fifteen roentgenograms; 2 photographs; 4 diagrams.

GERHART S. SCHWARZ, M.D.
New York, N. Y.

Quantitative Assay of Intrinsic Factor Activity by Urinary Excretion of Radioactive Vitamin B_{12}. Leon Ellenbogen and William L. Williams. Blood **13:** 582–588, June 1958. (American Cyanamid Company, Pearl River, N. Y.)

A technic for assaying consecutively up to 18 intrinsic factor preparations on the same pernicious anemia patient is described. Successive tests were made possible by the use of vitamin B_{12} labeled with Co^{60}. The use of repeated flushing doses of the vitamin appeared to have little effect on the response in the urinary excretion test; 9 patients were given up to 38 flushing doses of 1 mg. of nonradioactive B_{12} over a period of forty-four days and showed essentially the response to a standard

intrinsic factor preparation at the beginning and end of this period.

The excretion of vitamin B_{12} in the test increased with increasing amounts of intrinsic factor in each of four different preparations, indicating that large amounts of intrinsic factor did not inhibit absorption. There was no relationship between the urinary excretion values obtained with radioactive B_{12} alone and the values obtained with radioactive B_{12} plus standard intrinsic factor in a series of tests on 127 pernicious anemia patients. It appears that total rather than net excretion values are to be preferred in evaluating preparations. Since it has been shown that pernicious anemia patients given intrinsic factor absorb more than 0.5 μg. of radioactive vitamin B_{12}, an oral dose of 2.0 μg. of B_{12} which allows an absorption of more than 0.5 μg. is preferred in order to extend the range of intrinsic factor test doses that can be assayed.

Four tables. AUTHORS' SUMMARY

The Preoperative Irradiation of Breast Cancer with Radioactive Colloidal Gold (Au^{198}). Masao Okuhara, Ryoichi Monma, Koji Onoda, Tomokichi Takeda, and Takashi Honda. Am. J. Roentgenol. **79:** 988–993, June 1958. (M. O., Cancer Research Center, Kanazawa, Ishikawa, Japan)

The authors employed a colloidal suspension of radioactive gold in 8 cases of cancer of the breast. In each case the diagnosis was established by histologic examination of a biopsy specimen before the injection of the isotope. From 20 to 50 mc of radioactive gold (in a concentration of 1 mc per 1 c.c.) is injected into the cancerous breast, with an attempt to obtain as uniform a distribution as possible. Eight to ten peripheral sites are usually selected for injection.

Radical mastectomy was performed two to three weeks after the intramammary injection. The usual finding at the time of operation was a blackish-purple discoloration of the subcutaneous and fatty tissue in the breast and regional lymph nodes due to the deposition of the colloidal gold.

The authors have calculated that the intramammary injection of 50 mc of radioactive gold delivered to the central portion of the breast from 7,500 to 15,000 rep of beta radiation and 1,370 to 2,250 r of gamma radiation. About one-half of the axillary nodes received a dose of 7,600 rep and a dose of 257 to 284 gamma roentgens. When lymph nodes are not completely blocked by cancer cells, the radiogold can be deposited in them and yield a dose up to 35,000 rep of beta radiation.

Histologic sections after the injection of the mammary gland demonstrated radiation damage to the cancer cells, but the authors make no claim as to the destruction of the cancer in the breast or lymph nodes by radiation from the radioactive gold. The method does not appear to have any striking side-reactions and no significant complications were noted No long term follow-up is reported on these patients.

Five photomicrographs; 2 tables.

J. P. CHAMPION, M.D.
Grand Rapids, Mich.

Effect of Tranquilizing Agents on Radioactive Iodine Uptake in the Thyroid Gland. Morris T. Friedell. J.A.M.A. **167:** 983–984, June 21, 1958. (108 S. Michigan Ave., Chicago 3, Ill.)

It has been noted that a certain number of patients without evident thyroid enlargement or symptoms of hyperthyroidism other than anxiety show an elevated I^{131} uptake. A group of 12 such patients was subjected to a double blind study with placebo, meprobamate (Miltown), and meprobamate plus benactyzine hydrochloride. The results indicate that the tranquilizing agents may reduce tension or anxiety symptoms sufficiently to decrease the thyroid activity and therefore reduce the I^{131} uptake.

One table. GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

Comparison of the Uptake of Radioactive Iodinated Human Serum Albumin by Liver Tissue and Liver Metastases; Report of Four Human Cases. Douglas W. MacEwan. Am. J. Roentgenol. **79:** 1001–1003, June 1958. (3534 University St., Montreal 2, Que., Canada)

The author reports an attempt to evaluate the selective concentration of radioactive human serum albumin in metastatic cancer of the liver. Four patients were studied, 2 with carcinoma of the stomach and 2 with carcinoma of the breast. They had been injected with iodinated human serum albumin from eleven to forty-four hours prior to death.

At autopsy the liver was carefully dissected and comparison counts were made by means of a scintillating counter over metastatic areas as well as over normal liver tissue. The normal liver tissue was taken as far from the area of metastatic involvement as possible. There was no significant difference in the total number of counts obtained over the cancer tissue as compared to the normal liver tissue.

One table. J. P. CHAMPION, M.D.
Grand Rapids, Mich.

The Uptake of Radioactive Rubidium (Rb^{86}) by Breast Tumors. David M. Sklaroff. Am. J. Roentgenol. **79:** 994–998, June 1958. (5500 Old York Road, Philadelphia 41, Penna.)

An attempt was made to differentiate malignant and benign breast tumors by superficial counting over the tumor after the intravenous injection of a tracer dose of radioactive rubidium. Twenty-four malignant tumors and 11 benign tumors, all histologically verified, were evaluated. In addition to the preoperative counting, the material removed at the time of surgery was accurately counted and an attempt was made to correlate the two approaches.

It was found that more of the rubidium entered the malignant tumors than normal breast tissue; the benign tumors also showed an increased uptake, although less marked. On the average the uptake of malignant tumors was approximately ten times as great, and of benign tumors four times as great, as that of normal tissue. However, the degree of difference was, on the whole, too small, and the overlap between the benign and malignant tumors too great, for accurate preoperative diagnosis.

One graph; 3 tables. J. A. GUNN, M.D.
Grand Rapids, Mich.

Erythrocyte Survival in Leukemia, Hodgkin's Disease and Malignant Lymphoma as Determined by Radiochromate. Ronald E. Waggener, Peyton T. Pratt, and Howard B. Hunt. Am. J. Roentgenol. **79:** 1045–1049, June 1958. (University of Nebraska College of Medicine, Omaha 5, Nebr.)

In patients with leukemia, Hodgkin's disease, and malignant lymphoma, anemia is a common major prob-

lem. Its pathogenesis may be related to defective hematopoiesis, blood loss, or a reduced red blood cell survival time. The role of this last factor is not always obvious and requires special study for detection. The authors injected sodium radiochromate to tag the red cells and then obtained serial counts from the patient's blood to determine the erythrocyte half-survival time.

Patients with leukemia, Hodgkin's disease, and lymphoma were shown to have an erythrocyte half-survival time which varied from 50 to 60 per cent of normal. Correlation was made with other tests and it was found that the reticulocyte count when elevated above 2 per cent suggests an accelerated destruction of red blood cells. Bile pigment studies failed to reveal accelerated red blood cell destruction.

Approximately half of the patients with a reduced red blood cell survival time were without splenomegaly. It was also found that patients receiving roentgen therapy showed slightly shorter average erythrocyte survival time than those patients who were not receiving irradiation at the time of the study. One patient with serious reduction in erythrocyte survival time showed a normal index approximately four months after completion of x-ray therapy.

One figure; 3 tables. J. A. GUNN, M.D.
Grand Rapids, Mich.

Evidence of Central Nervous System Influence Upon Cold-Induced Acceleration of Thyroidal I^{131} Release. Karl M. Knigge and Stanley M. Bierman Am. J. Physiol. **192:** 625–630, March 1958. (School of Medicine, University of California, Los Angeles, Calif.)

When animals are subjected to low environmental temperatures, there results, during the initial period of exposure, a marked acceleration of the release of thyroidal hormone, a phenomenon which may be dependent upon neural stimulation of thyrotropin secretion (see Knigge *et al.*: Am. J. Physiol. **189:** 415, 1957. Abst. in Radiology **70:** 628, 1958). The present paper reports experiments undertaken to explore further this aspect of central nervous system influence upon thyroid function.

It was found that during the initial twelve hours of cold exposure (5° C.) of the hamster, thyroidal I^{131} release was markedly accelerated. This response was not influenced by bilateral nephrectomy, adrenal demedullectomy, or adrenalectomy. Treatment of animals with reserpine and hypothalamic damage by appropriately placed median eminence lesions twenty-four hours before exposure or chronic lesions (three to six weeks) did not interfere with subsequent normal hormone delivery but did block the accelerated release attendant upon cold exposure. In hypophysectomized hamsters, I^{131} uptake was restored to normal by treatment with TSH. After this uptake was achieved and exogenous TSH discontinued, release from the thyroid was slow and could not be accelerated by cold. Transplantation of fragments of one-half to two pituitary glands into the cheek pouch of hypophysectomized hamsters temporarily restored both uptake and release. Cold exposure, however, did not accelerate thyroidal release in such graft-bearing animals.

These experiments indicate that upon cold exposure a central nervous system stimulus is responsible for triggering the pituitary-thyroid system and that the accelerated thyroidal I^{131} delivery, depending upon increased secretion of TSH, requires adenohypophyseal tissue with its normal anatomical connections to the hypothalamus.

Six figures.

Renal Excretion of Radioiodide in Rats. N. S. Halmi, L. T. King, R. R. Widner, A. C. Hass, and R. G. Stuelke. Am. J. Physiol. **193:** 379–385, May 1958. (State University of Iowa, Iowa City, Iowa)

Elimination of radioiodide by the kidney of adult male rats pretreated with a single dose of propylthiouracil was measured. Rats given water or isotonic saccharose served as controls. Renal clearance of radioiodide ($C_{I^{131}}$) was greatly enhanced (up to 100-fold) by the sodium salts of chloride, perchlorate, stable iodide, bromide and bicarbonate, and by choline iodide, but not by sodium thiosulfate. Under most conditions, $C_{I^{131}}$ markedly exceeded the C_{Cl} and C_{Na} of the same animals, which suggests that renal tubules are less permeable to iodide than to chloride or sodium. $C_{I^{131}}/C_{Na}$ varied greatly, its magnitude being dependent on the loading solution used. $C_{I^{131}}$ showed no correlation with urine flow or excretion of endogenous creatinine-like chromogen ($U_{Cr}V$) when groups receiving different treatments were compared. Both urine flow and $U_{Cr}V$ revealed only minor variations among these groups. The authors' findings are most easily explained by the hypothesis that tubular reabsorption of iodide filtered by the glomeruli involves, possibly in addition to a passive process, an active transport mechanism capable of saturation by iodide and (competitive?) inhibition by other anions.

Three figures; 2 tables. AUTHORS' ABSTRACT

Enhancement of Vitamin B_{12} Absorption by D-Sorbitol as Measured by Maternal and Fetal Tissue Levels in Pregnant Rats. Edward G. Rice, John F. Herndon, Edward J. Van Loon, and Samuel M. Greenberg. Am. J. Physiol. **193:** 513–515, June 1958. (Smith, Kline and French Laboratories, Philadelphia, Penna.)

Tissue vitamin B_{12} levels were determined in the blood, liver, kidneys, gastrointestinal tract, and uteri and contents in pregnant and nonpregnant female rats following oral administration of three doses of radioactive vitamin B_{12} (Co^{60}). Differences in radioactivity of tissues of animals given Co^{60} vitamin B_{12} in water and in D-sorbitol at different stages of pregnancy were noted. D-Sorbitol administration significantly enhanced vitamin B_{12} absorption in both pregnant and nonpregnant rats. Gestation, but not D-sorbitol, causes an alteration of the tissue distribution pattern of the vitamin. As fetal growth progressed, the fetuses obtained a large proportion of the absorbed B_{12} which would normally have gone to the maternal tissues. During growth of the total fetal mass from 3 to 30 gm. the amount of B_{12} retained per gram of tissue remained fairly constant. The amount of B_{12} taken up by the fetuses was to a great degree controlled by the amount absorbed by or stored in the mother during gestation.

Three figures; 1 table. AUTHORS' ABSTRACT

Blood Volumes of Dairy Calves Comparing Cr^{51}-Tagged Red Blood Cells and T-1824 Plasma Dilution Methods. Perry Ruth Stahl and Homer E. Dale. Am. J. Physiol. **193:** 244–248, May 1958. (Division of Agricultural Science, University of Missouri, Columbia, Mo.)

In a repeated study on 17 dairy calves, the T-1824 dye plasma dilution technic showed significantly higher

blood volumes than were found by any other technic or computation method using Cr^{51}-tagged red blood cells. Five blood samples taken at twenty-minute intervals after injection revealed consistent decrease in radioactivity count from the first to the last sample, indicating greater accuracy in radioactivity dilution regressed to zero time figures than in average counts of several postinjection samples.

In vitro studies suggest a loss of Cr^{51} from red blood cells to plasma after saline washings are Cr-free. Percentage blood volumes computed from whole blood samples of calves injected with Cr^{51}-tagged red blood cells decreased in a straight line relationship with increase of body weight. Percentage plasma and whole blood volumes estimated with the T-1824 dye technic decreased regularly with body weight increase until a second determination was made, when there was a rapid rise nearly to the level of the smallest calves, followed by another regular decrease with increase in weight.

It is suggested that repeated dye injections do not always measure the same space. Regressed values of five whole blood samples taken at twenty-minute intervals after injection of Cr^{51} tagged red blood cells gave more consistent blood volume determinations than either the weighed red cells or the plasma dye dilutions of the same samples.

Three graphs; 2 tables. AUTHORS' ABSTRACT

RADIATION EFFECTS

X-Irradiation Effects on the Human Fetus. Roberts Rugh. J. Pediat. **52**: 531–538, May 1958. (Radiological Research Laboratory, Columbia University, New York 32, N. Y.)

Information relative to the stage in fetal development and the exposure level at which irradiation will cause demonstrable abnormalities is discussed. When one plots the sequence of organogenesis in the mouse or rat with that of the human embryo, using the two time scales, it is obvious that development of these mammalian forms is basically similar. Every irradiation-produced abnormality in the human fetus has been experimentally produced in the mouse or rat embryo following irradiation at a comparable stage of development, and it is considered justifiable to extrapolate from these animals in regard to specific organ susceptibility periods with the proviso that any statement is prefixed with the word "probable."

The most radiosensitive period in the entire prenatal life probably occurs between the eighteenth and thirty-eighth days, for it is during this time that all of the organ primordia are laid down by rapid differentiation from primitive cell types. After day the thirty-eighth higher levels of exposure are necessary to produce anomalies, teratologies becoming less common.

Caution in regard to fetal irradiation at any time is urged for three reasons. (1) There is danger of damage to germ cells, genetic effects of irradiation probably beginning shortly after the thirty-second day, when the genital ridges first appear, and continuing through the reproductive span of the individual. (2) Injury to scattered neuroblasts with advancing fetal age may bring effects which are more subtle; however, neural insufficiency and other nervous disorders can be the result of this neural deletion. (3) It is known that prenatal irradiation increased the probability of leukemia in young children, even though a linear relation is yet unproved.

Brief discussion is devoted to instances of survival following high fetal dosage without gross abnormality at birth. In some cases there has been subsequent evidence of abnormal psychological behavior, supporting the thesis that there may be functional damage at levels too low to have structural corollaries. There can be no controls for these data, the range of human normality being so great that, even if a child's potential IQ is reduced from 140 to 70 by fetal irradiation, he would still be considered as normal. The author states that we simply cannot evaluate the deleterious effects of irradiation of the fetus, for there are sequelae which are not evident for many years, affecting future generations, even beside genetic mutations. Included are: shortening of life, the development of cancer, cataracts, sterility, increased susceptibility to disease, and numerous less evident factors which affect survival.

The author concludes that irradiation of the pregnant woman, particularly in the early trimester, should be discouraged under all conditions short of saving her life. Further, it would be a wise practice to determine the time of the prior menses in all radiological examinations of women in order to avoid the possibility of exposure of an unrecognized pregnancy during the most radiosensitive period, at about 2.5 to six weeks.

Two illustrations; 2 tables.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

A Survey of Childhood Malignancies. Alice Stewart, Josefine Webb, and David Hewitt. Brit. M. J. **1**: 1495–1508, June 28, 1958. (Department of Social Medicine, Oxford University, Oxford, England)

Data are presented from an extensive survey in which an attempt was made to trace and record the histories of all children under ten years who died from leukemia or other malignant disease in England and Wales during the years 1953 to 1955. Most of the findings are based on 619 cases of leukemia and 680 other cancers, with a carefully selected control group of children matched for age, sex, and locality but otherwise chosen at random from the local birth register.

Information was obtained as to diagnostic abdominal roentgen examinations on mothers during the relevant pregnancy, and it was found that children exposed to radiation *in utero* are twice as likely to die of a malignant disease before the age of ten as are other children. It is estimated, however, that less than one in a thousand of the prenatal x-ray examinations in recent years have led to death from malignant disease.

Analysis of postnatal x-ray exposure suggested two reasons for thinking that the taking of x-ray films shortly after birth influences the distribution of childhood deaths from malignant disease. In the first place, there is a significant case excess for x-ray exposures during infancy. Secondly, children who died of leukemia at the ages of two and three were concentrated within the group exposed to radiation in infancy. The effect of postnatal x-ray exposure appears to be more marked in respect to leukemia than other cancers and to be much weaker than the effect of prenatal exposure. It may, in fact, be restricted to speeding the date of

death in children already predisposed to leukemia. Lack of association between the parts of the body exposed to x-rays and subsequent developments may be related to the fact that in infancy the reticuloendothelial system is so widespread that it is likely to be involved in any exposure.

Development of malignant disease in this series had no relationship to locality, maternal illnesses, exposure to other ionizing radiation (television sets, luminous toys, pedoscopes), feeding habits, or use of sulfonamides and antibiotics. On the other hand, excessive maternal age, with or without x-ray exposure, appears to increase the risk of leukemia in childhood. Mothers over the age of forty represented 6.9 per cent of the leukemic series and only 3.5 per cent of the other cancer series. Moreover, the significantly higher incidence of mongolism in the children of older mothers suggests that childhood leukemia and mongolism are influenced by a common factor.

The authors conclude that "fetal irradiation does not account for the recent increase in childhood malignancies, but the finding of a case excess for this event does underline the need to use minimum doses for essential medical x-ray examinations and treatments."

One diagram; 27 tables.

LAWRENCE A. POST, M.D.
University of California, S. F.

Radiobiologic Observations on Cancer Patients Treated with Whole-Body X-Irradiation. Lowell S. Miller, Gilbert H. Fletcher, and Herbert B. Gerstner. Radiation Res. **8:** 150–165, February 1958. (M. D. Anderson Hospital, Houston, Texas)

Radiobiologic observations on a series of 263 cancer patients given whole-body x-irradiation are presented. Critical evaluation of the procedure as a therapeutic tool will be the subject of another report; the present article is limited essentially to a discussion of the acute and subacute effects, so far as they were systemic in nature. The first 233 patients were exposed to doses ranging from 15 to 200 r and the last 30 to 200 r.

Systemic effects induced in human beings by whole-body x-irradiation occur in two phases. The first, the initial reaction, is characterized by fatigue, anorexia, nausea, and vomiting. In typical cases it begins approximately two hours after exposure and subsides twenty-four hours later. As shown by Court Brown (Brit. M. J. **1:** 802, 1953), a strong psychologic component may frequently be involved. The second phase, a more or less pronounced bone marrow depression, is characterized by a tendency toward bleeding, infection, and pancytopenia. In typical cases, it becomes significant clinically three to four weeks post-irradiation and begins to subside six to eight weeks after exposure. Generally, doses of 100 r or lower are subthreshold and will not produce these reactions. In the dose range between 125 r and 175 r the two phases begin to appear in about 50 per cent of the cases; the reactions are too mild, however, to demand countermeasures other than psychologic reassurance. At 200 r, the two phases are clearly recognizable in about 80 per cent of the cases, and the reactions are sufficiently severe to require clinical treatment in about 10 per cent of the patients. Thus the threshold dose beyond which, in a small percentage of patients, serious complications begin to appear, lies somewhere between 150 and 200 r.

Seven illustrations; 6 tables.

Intraosseous Cystic Lesion Caused by Schwannoma. K. S. Bose. J. Indian M. A. **31:** 290–291, Oct. 1, 1958. (Medical College Hospitals, Calcutta, India)

The author presents a case of a schwannoma causing an erosive defect in the ilium of a 22-year-old male. Roentgen studies on Nov. 1, 1957, showed a cystic lesion near the iliac crest. The margins of the radiolucent area were clear-cut and slightly sclerosed, and it was the radiologist's opinion that the lesion might be a healed osteomyelitis or fibrous dysplasia. Biopsy section on Jan. 29, 1958, demonstrated a schwannoma.

One photomicrograph.

Cortisone and the Treatment of Radiation Sickness. R. Finney. J. Fac. Radiologists **9:** 68–79, April 1958. (Newcastle General Hospital, Newcastle, England)

The value of cortisone in the management of radiation sickness was studied in 32 cases of spinal arthritis (ankylosing spondylitis or osteoarthritis), treated by irradiation of the whole spine and sacroiliac joints. A total dose of 1,500 r was given in five treatments over fourteen days overall time. The series was randomized, 16 patients receiving cortisone and 16 identical "dummy" tablets. The dosage of cortisone employed was 150 mg. daily in divided doses, commencing forty-eight hours prior to irradiation and continuing throughout the fourteen days of the course of treatment, after which 75 mg. in divided dosage was given for three days, then 25 mg. for a further three days. The following observations were made:

The latent period in patients in whom symptoms of radiation sickness developed under cortisone cover was increased by about 70 per cent over the control group—a difference statistically significant.

Symptoms of any type were much less frequent and less severe under cortisone than without, and furthermore the rate of decrease of symptom frequency was appreciably more rapid in the former group. There was a greater tendency toward the occurrence of a single disturbance in the cortisone series. There was a relief of all symptoms in a higher percentage of cases with cortisone as compared with the controls, but only in the case of anorexia, headache, and nausea was the difference statistically significant. In both groups nausea and malaise remained the most lasting of the various disturbances.

A "protector" effect from cortisone on the peripheral blood-count was demonstrated by a lesser fall in the total white-cells during irradiation.

Cortisone had no effect on the mild first degree erythema resulting from the quantity and quality of irradiation administered.

The actual figure obtained in the cortisone series for the complete relief of symptoms was only 37.5 per cent and therefore it must be concluded that lack of cortisone does not appear to be the immediate cause of radiation sickness, although undoubtedly significant modifying changes do occur after its administration.

Fourteen figures; 4 tables.

Variability of the In Vitro Sensitivity of Human Leukemic Lymphocytes to X Rays and Chemotherapeutic Agents. Robert Schrek, Irving A. Friedman, and Stanley L. Leithold. J. Nat. Cancer Inst. **20:** 1037–1050, June 1958. (VA Hospital, Hines, Ill.)

A slide-chamber method was used to test 31 patients with chronic lymphocytic leukemia for the sensitivity of their blood lymphocytes to x-rays and radiomimetic

drugs *in vitro*. The results of the radiosensitivity tests were expressed as 10 per cent ST-1000 r, *i.e.*, the 10 per cent survival time of the cells after treatment with 1,000 r.

Repeat tests on the same patients showed good reproducibility of the determinations of 10 per cent ST-1000 r. The patients differed in the sensitivity of their blood lymphocytes to x-rays with the 10 per cent ST-1000 r varying from 0.3 to 10+ days. The effect of 10 to 1,000 r of x-rays on the 10 per cent survival time was represented by dose-effect curves, which were found to vary for different patients with respect to position, shape, and slope. The lymphocytes of the patients also varied in their sensitivity to nitrogen mustard (HN_2) and triethylenemelamine (TEM). Nineteen patients were tested with two or three reagents. A significant correlation was found between the sensitivity of a patient's lymphocytes to x-rays and to nitrogen mustard.

Eight figures; 3 tables. AUTHORS' SUMMARY

EXPERIMENTAL STUDIES

Mechanism of Emesis Following X-Irradiation. S. C. Wang, A. A. Renzi, and H. I. Chinn. Am. J. Physiol. **193:** 335–339, May 1958. (College of Physicians and Surgeons, Columbia University, New York 32, N. Y.)

Chinn and Wang showed that dogs exposed to 800 r total-body irradiation vomited within two hours after completion of the exposure (Proc. Soc. Exper. Biol. & Med. **85:** 472, 1954). After chronic destruction of the chemoceptive emetic trigger zone, no dog vomited within two hours of radiation. More recently it has been observed that these operated dogs would vomit later in the post-irradiation period. Some dogs vomited continually, but more often they exhibited an initial vomiting response and then did not vomit again until death was imminent. Visceral deafferentation alone (abdominal vagotomy and sympathectomy) did not keep dogs from vomiting soon after irradiation or within several days. On the other hand, both acute and delayed emesis due to irradiation was not seen in dogs with chronic destruction of the chemoceptive trigger zone and abdominal visceral deafferentation. It appears, therefore, that delayed vomiting following lethal total-body irradiation is mediated through two mechanisms: the centrally located trigger zone and the peripheral visceral afferent receptors of the vagus and sympathetic trunks.

Five tables.

Roentgen-Induced Carcinoma of the Rat Tail. Ernst Stutz and Ursula Blüthgen. Strahlentherapie **105:** 278–295, February 1958. (Universität Freiburg/Br., Germany)

The tails of 344 rats were irradiated with x-rays. Contrary to the opinion of Rowntree (Lancet **1:** 821, 1909), who held that carcinoma cannot be induced in the rat tail by irradiation, it was found that carcinoma could be produced if the fractionation of the exposure was favorable.

The total dose was less important for the result than the mode of fractionation. Thus, daily doses of 50 to 150 r delivered throughout one year for total doses of 15,000 to 60,000 r failed to produce carcinoma. On the other hand, total doses of as little as 10,000 r sufficed when delivered in daily doses of 500 r within three weeks. A single dose of 4,000 r followed by additional fractionated treatment yielded the highest incidence of tumors. The rat tail is considered an ideal test object by the authors, because it is never the site of spontaneous tumors.

The latency period of the artificially induced carcinomas varied between seventeen and twenty-seven months. Factors 140 kv, 0.25 mm. Al h.v.l.

One photomicrograph; 10 photographs; 1 table.

GERHART S. SCHWARZ, M.D.
New York, N. Y.

Total-Body Irradiation and Allyl Alcohol Damage of the Liver; A Study of the Change in Resistance of the Body Caused by X-Irradiation. Wilhelm Eger and Christa Terruhn. Strahlentherapie **105:** 296–306, February 1958. (Pathologische Institut, Universität Göttingen, Germany)

Rats were exposed to a single dose of x-rays (180 to 200 kv; h.v.l. 0.5 to 1.13 mm. Cu; 84 to 132 r/min. of between 15 and 1,500 r with most receiving 250 r. The liver was damaged with allyl-alcohol or carbon tetrachloride 3, 5, 7, 14, 28, 56, and 112 hours prior to the exposure. Some of the rats were pretreated with Zymosan and Dextran in an effort to keep the properdin level up. (Properdin is a gamma globulin fraction which is said to help in the resistance against post-radiation infection.)

The surprising and paradoxical finding was that total-body irradiation *increased* the resistance against liver damage. The higher the x-ray dose, the greater the protection. Maximum protection was found when the x-rays were delivered seven to fourteen hours after the intoxication. The interval between poisoning and irradiation must be less than twenty-eight hours to show an effect.

Two photomicrographs; 2 diagrams; 1 table.

GERHART S. SCHWARZ, M.D.
New York, N. Y.

Effect of X-Ray Irradiation on Muscle Fatigue in Rats. Thomas J. Haley, A. M. Flesher, N. Komesu, E. F. McCulloh, and W. G. McCormick. Am. J. Physiol. **193:** 355–359, May 1958. (School of Medicine, University of California, Los Angeles, Calif.)

With the Ingle fatigue test (see Endocrinology **34:** 191, 1944) the authors have demonstrated that a loss of muscle responsiveness, increased fatigability, and decreased work output in the rat follow 600 r acute whole-body x-irradiation. These effects increase with time post-irradiation. In both normal and irradiated animals, strain differences were observed. The administration of adrenocortical extract did not improve performance, and no improvement in this respect could be seen in adrenalectomized animals given cortical extract. It is postulated that the poor performance of the irradiated animals is related to a lack of glycogenolysis, poor intestinal absorption of glucose, and circulatory collapse.

Postirradiation Parabiosis: Influence of Myleran on Protection. Martin Schneider, William E. Watson, Carroll C. Jones, and John C. Finerty. Radiation Res. **8:** 227–233, March 1958. (University of Texas Medical Branch, Galveston, Texas)

The effect of Myleran on parabiotic protection against the effects of 700 r total-body x-irradiation was studied in female rats. None of the irradiated rats

survived if paired with Myleran-injected animals. This mortality is in contrast with a 60 per cent survival in irradiated animals paired with normal partners. In the dosage used (20 mg./kg.), Myleran was not fatal to single rats. Injected in one parabiont, it had no effect on survival of the nonirradiated partner beyond the expected mortality of these parabionts from "parabiosis intoxication."

Irradiated rats suffered a drastic reduction in leukocytes within two days. The irradiated normal partners showed a return of total leukocyte count and of lymphocyte and neutrophil counts to a normal level in nine days. Parabionts, injected with Myleran prior to functional anastomosis with a normal rat, showed the same initial depression as single rats, but a more rapid return to the normal level (six days contrasted to fourteen days), attributed to the large flow of blood between the normal and injected animals after capillary inoculation. In both partners there was profound depression and death after failure of adequate recovery of the total leukocyte, lymphocyte, and neutrophil levels when an irradiated rat was joined to a nonirradiated Myleran-injected rat.

Six graphs; 1 table.

Nonspecific Protective Effect of Small Lead Shields Against Irradiation Death in the Rat. David F. Bohr, P. A. Rondell, L. E. Palmer, and Frank H. Bethell. Am. J. Physiol. **193:** 95–97, April 1958. (Department of Physiology, University of Michigan, Ann Arbor, Mich.)

Studies by the authors showed that rats subjected to 650 r whole-body x-irradiation are protected, and to about equal extent, by shielding either skin or muscle tissue. Shielding both tissues virtually doubled the protection. These findings support the hypothesis (Bohr, *et al.*: Am. J. Physiol. **183:** 335, 1955. Abst. in Radiology **67:** 647, 1956) that various tissues, if shielded, are capable of contributing to the animal some form of protection which will significantly decrease the lethal effects of irradiation. The fact that the type of tissue shielded does not greatly influence the degree of protection suggests that this contribution may be a potentiality of any unirradiated cell and not related to the primary physiologic function of the shielded tissue. The mechanism of this protection is not obvious. It may be due to circulating humoral substances having their origin in the shielded tissue and exerting a protective or recuperative effect on the irradiated tissue. Or, if the postirradiation syndrome is aggravated by circulating noxious materials, it is conceivable that the contribution may be made by the inactivation of such material by the unirradiated tissue.

One table.

Strain Differences in Response to Whole Body Irradiation and Shielding Procedures in the Rat. David F. Bohr, C. Zippin, P. A. Rondell, and L. E. Palmer. Am. J. Physiol. **193:** 98–100, April 1958. (Department of Physiology, University of Michigan, Ann Arbor, Mich.)

Over the past three years the authors have used 421 rats in studies of the protective effect of lead shields against irradiation death (see preceding abstract). Two strains of rats were used throughout these studies. The strain that was more sensitive to whole-body x-irradiation was also the one more effectively protected by the shielding procedure. Previous work indicated that shielded tissues make some contribution to the irradiated animal which enhances its chances of survival. From the current experiments it is concluded that the strain in which the tissues are best able to make this type of contribution is also the one in which this contribution is most readily destroyed by irradiation.

One table.

Chronic Radiation Mortality in Mice after Single Whole-Body Exposure to 250-, 135-, and 80-kvp X-Rays. Douglas Grahn and George A. Sacher. Radiation Res. **8:** 187–194, February 1958. (Division of Biological & Medical Research, Argonne National Laboratory, Lemont, Ill.)

The comparative acute lethal response of mice exposed to three different x-ray qualities has been established (Radiation Res. **4:** 228, 1956. Abst. in Radiology **68:** 474, 1957). Animals that survived acutely lethal doses were kept for duration of life to compare the three radiation qualities in terms of chronic radiation injury and mortality. The term "chronic" is used to define the late or delayed deaths after irradiation and does not refer to a physical pattern of radiation exposures.

Mice subjected to equal acute injury by exposure to 250-kvp, 135-kvp, or 80-kvp x-rays were found to show a uniform degree of chronic injury. Mean after-survival and tumor incidence were the same for all radiation qualities. Females demonstrated a greater sensitivity to chronic radiation injury than males. Reduction of life expectancy after dosages in the midlethal range averaged 36.7 per cent and 29.2 per cent for females and males, respectively. In the x-ray energy range of 80 to 250 kvp, the values for comparative effectiveness derived from acute LD 50/30 air doses are concluded to be equally valid for measuring effectiveness in terms of chronic injury and mortality after single-dose whole-body exposure.

Two illustrations; 4 tables.

The Relative Biological Effectiveness of Fission Neutrons for the Production of Acute Mortality in Mice. Nicholas Delihas and Howard J. Curtis. Radiation Res. **8:** 166–180, February 1958. (Brookhaven National Laboratory, Upton, N. Y.)

During the past twenty years a number of scientific investigators have performed experiments to determine the relative biological effectiveness (RBE) of fast neutrons in the production of acute lethality in mice. Conflicting values have been reported and Boag (National Bureau of Standards Report 2946, 1953) has given some explanations as to the possible sources of error and difficulties in most of these studies. Up to the present, the RBE for neutrons is still unsettled, and a complete explanation of the difficulties involved in this situation has yet to be found. The purpose of the present report is to describe the methods and technics used by the authors in determining their value for the RBE of fission neutrons. Since the neutron dose has been one of the major sources of discrepancy, they tried to use the most efficient and direct method for its measurement, *i.e.*, the tissue-equivalent ionization chamber.

The importance of determining an RBE for various radiations is twofold: it can aid in the establishment of maximum permissible exposures of human beings to these radiations, and it can contribute to an understanding of the basic mechanism by which radiation interacts with living cells and tissues.

In the authors' studies, an RBE of 1.7 of fission neutrons with respect to 250-kvp x-rays to produce an LD 50 in thirty days in CF_1 female mice was obtained. The x-ray LD 50 dose was 636 rads, and the neutron dose was 366 rads.

Seven illustrations; 5 tables.

Bacteriological Studies on Mice Exposed to Supralethal Doses of Ionizing Radiations. II. Fast Neutron and X-Radiation from Laboratory Sources. Myron S. Silverman, Vivian Greenman, Paul H. Chin, and Victor P. Bond. Radiation Res. **8:** 123–130, February 1958. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

In an earlier article, the authors presented evidence showing that a high percentage of mice exposed to doses of fast neutron radiation or combined neutron and γ-radiation from a nuclear device were infected with endogenous enteric bacteria at the time of death (Radiation Res. **7:** 270, 1957. Abst. in Radiology **71:** 317, 1958). The doses to which the animals were exposed were sufficient to result primarily in gastrointestinal injury and death within five days. These findings were contrary to those described by others, who reported little or no infection in mice exposed to corresponding doses of ionizing radiation from laboratory sources. Since it was necessary in the previous experiment to sacrifice the animals when moribund, the possibility that a preagonal invasion had occurred could not be eliminated. More extensive studies have been undertaken to determine the role of infection in the death of the animals.

Infection with one or more species of endogenous enteric bacteria was found to occur in a high percentage of mice after exposure to supralethal doses of neutron radiation (510 rads) or x-radiation (1,340 rads), doses which result in death within five days probably from gastrointestinal injury. The incidence of infection paralleled the increase in deaths. During the first sixty hours bacteria were isolated primarily from the spleen. After that time a bacteremia developed.

The administration of 10 mg. of streptomycin and 4,000 units of penicillin drastically decreased the incidence of infection but did not alter the percentage of deaths or the mean survival time of the neutron-irradiated mice, although the mean survival time of the x-irradiated mice was lengthened somewhat. Hence, it must be concluded that post-irradiation infection plays only a minor role, if any, as a cause of death after exposures to these doses of ionizing radiation.

Two graphs; 4 tables.

Effect of Daily Gamma-Irradiation on the Pigmentation of Mice. Walter C. Quevedo, Jr. and Douglas Grahn. Radiation Res. **8:** 254–264, March 1958. (Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill.)

During the course of survival studies it was observed that in certain pigmented mice undergoing daily γ-irradiation, a marked hyperpigmentation of the extremities developed, and in some cases a graying of the body hairs. Both phenomena are indicative of an underlying change at the cellular level—an alteration of melanocyte activity. The present paper deals with the fate of melanocytes during continued exposure to both x- and γ-rays, particularly with regard to the production of hyperpigmentation.

It was found that when LAF_1 and C57BL mice were exposed for the duration of life to daily doses of γ-rays ranging 6 r/day to 410 r/day, the extremities became progressively darkened. With doses ranging from 6 r/day to 170 r/day, the magnitude of hyperpigmentation appeared to be a function of both radiation intensity and total accumulated radiation dose.

Experiments with one foot of an animal shielded showed that hyperpigmentation results from a direct action of x- and γ-radiation.

Radiation-induced hyperpigmentation arises from an increased amount of epidermal melanin associated with increased melanogenic activity of melanocytes in the basal layer of the epidermis.

Graying of the pelage, indicative of a loss of follicular melanocytes, also occurs in daily irradiated mice exhibiting hyperpigmentation of the extremities.

The bearing of these observations on general problems of pigment-cell dynamics is discussed.

Six illustrations; 1 table.

Hematopoietic Recovery Induced by Bacterial Endotoxin in Irradiated Mice. Willie W. Smith, Ilo M. Alderman, and Ruth E. Gillespie. Am. J. Physiol. **192:** 549–556, March 1958. (National Cancer Institute, Bethesda, Md.)

The intraperitoneal injection of *Salmonella typhosa* endotoxin in mice twenty-four hours before irradiation (750 to 900 r x-rays from a Van de Graaff generator operating at 2.5 MEV, 0.6 ma, with h.v.l. 1 cm. lead) resulted in an advance in the recovery of granulocytes, platelets and hemoglobin. The effect on lymphocyte counts was relatively small. Differences in bone marrow cellularity and in ability to mobilize granulocytes were particularly striking. Effects of an injection given after irradiation, although significant, were less pronounced. The induction of hemopoiesis is thought to be responsible for the increase in survival previously observed with this treatment. It is not known whether the action of endotoxin upon the precursor cells is direct or indirect.

Seven illustrations; 1 table.

Failure of Pregnancy as a Protective Agent against X-Irradiation. J. F. Spalding, V. G. Strang, and S. B. Hawkins. Radiation Res. **8:** 222–226, March 1958. (Los Alamos Scientific Laboratory, Los Alamos, N. Mex.)

The findings of some investigators seem to show that gravid females, because of hormonal changes, are more resistant to ionizing radiation than nongravid females. On the other hand, the stress of pregnancy and parturition might be expected to lower the resistance to radiation. A study was undertaken to obtain the LD 50/15 and LD 50/30 of female CF_1 mice exposed to x-rays during the fourteenth to eighteenth days of gestation as opposed to the LD 50/15 and LD 50/30 of nongravid mice.

Two hundred and ten gravid and a like number of nongravid mice were exposed, in groups of 30, to whole-body x-ray tissue doses of 0, 438, 490, 547, 612, 684, and 766 rads. A record of litters kept on the gravid animals showed a decrease in litter size and live-to-dead ratio with increase in the x-ray dose.

The LD 50/15 for the gravid mice was 605.9 ± 11.1 and for the nongravid mice 608.7 ± 7.0; the LD 50/30 was 564.5 ± 11.7 and 581.8 ± 10.7, respectively. It is obvious that terminal stages of pregnancy on CF_1 mice afford no protective effect against x-irradiation which would increase the LD 50 at these times.

Immunological Characteristics of Radiation Chimaeras. P. L. T. Ilbery, P. C. Koller, and J. F. Loutit. J. Nat. Cancer Inst. **20:** 1051–1089, June 1958. (P. L. T. I., Department of Preventive Medicine, University of Sydney, New South Wales, Australia)

Radiation chimaeras are mice that due to bone-marrow therapy survive LD 100 total-body x-irradiation. The donor material may differ genetically from the irradiated recipient. According to the genetic relationship between the host and donor, radiation mouse chimaeras can be grouped as follows: isologous, semi-isologous, syngenetic, homologous, and heterologous.

The immunological responses of the various chimaeras have been analyzed by challenging them with different tumors. In *isologous chimaeras*, in which host and donor are of the same genetic constitution, *i.e.*, are members of the same strain (CBA/CBA), the donor marrow does not fully restore the immune mechanism of the irradiated host. The addition of lymph node to bone marrow as donor material shortened the immunologically neutral state of isologous chimaeras and almost completely restored immunity of the host to foreign tumor. In *syngenetic chimaeras*, which are composed of more than 2 strains, 1 or more of these being common to host and donor, the addition of lymph node to bone marrow as donor material fully restored natural immunity of host. In *homologous chimaeras*, in which host and donor belong to different strains, it was found that the animals were not neutral immunologically and that the immune mechanism was not controlled by the host alone. *Semi-isologous chimaeras* are mice of 1 of 2 inbred strains, *e.g.*, (A or C57BL) in combination with the F_1 hybrid. While immunity on the (A × C57BL)F_1 host was not conferredb y the marrow and lymph-node donor material of the parental strains that had been immunized against tumors of each other, bone marrow and lymph node of the F_1 hybrid seemed to confer susceptibility on mice of the parental strains for tumors of each other. A similar immunological response was demonstrated by chimaeras with hybrid constitution and by chimaeras that received *subacute* radiation. Chimaeras, when challenged by different tumors in succession, exhibited variable immune responses that may suggest tumor "enhancement," interaction, or differences in the proportion of host-donor cell population.

Chimaeras in which host and donor differ genetically show varying degrees of "secondary disease," depending on the extent of genetic divergence. Secondary disease is attributed to a *chronic* tissue antigen-antibody reaction. The early death of chimaeras that received bone marrow and lymph node as donor material is assumed on histological evidence to be due to a similar but acute tissue antigen-antibody reaction. Experimental evidence seems to indicate that the immune reaction is that of the *graft versus host*. It is argued that in chimaeras which survived or escaped secondary disease, the donor and host cells have become "nonreacting" *i.e.*, have been altered immunologically and have been adapted to an existence in "the symbiotic state."

Twenty photomicrographs; 2 charts; 10 tables.

AUTHORS' SUMMARY

Evidence of Circulatory Failure in the Early Radiation Response of the Chicken. S. P. Stearner, M. H. Sanderson, E. J. Christian, and A. M. Brues. Am. J. Physiol. **192:** 620–624, March 1958 (Argonne National Laboratory, Lemont, Ill.)

The early radiation syndrome in the chicken is distinct from that associated with death several days after exposure. In both young chicks and adult roosters, the mode of early death is characterized by a progressive circulatory collapse. To obtain more precise estimates of the circulatory changes in the initial post-irradiation period, the authors measured total peripheral blood volume and the blood volume of several visceral organs and of skeletal muscle. Determinations were made on control and x-irradiated chicks and adult roosters. In chicks the post-irradiation decrease in actively circulating blood volume ranged from 30 to 60 per cent. Previous studies of hemorrhagic hypotension in chicks have shown that loss of one-third of the circulating blood volume is sufficient to produce irreversible shock and renal failure. Roosters, however, can compensate for much greater loss in blood volume. Loss by hemorrhage of more than 60 to 70 per cent of the normal circulating volume is frequently required to produce irreversible shock. In x-irradiated roosters, values obtained from the peripheral blood indicated no decrease in volume of circulating red cells and a 30 per cent decrease in plasma volume. The distribution of erythrocytes and plasma, however, was significantly altered. The decrease in circulating blood volume was most marked in the liver, spleen, and kidneys and was probably sufficient to produce a significant effect on function.

Four graphs; 2 tables.

Effect of X-Irradiation on Bound Iron and Unsaturated Iron-Binding Capacity in Rabbits. Thomas J. Haley, Anna M. Flesher, and Nathan Komesu. Am. J. Physiol. **192:** 560–562, March 1958. (School of Medicine, University of California, Los Angeles, Calif.)

Previous studies have shown that acute whole-body x-irradiation in the rabbit produced a hyperferremia which was not modified by reticuloendothelial blockade or a sterile abscess, while local irradiation of the liver and spleen produced a hypoferremia. It has also been shown that whole-body x-irradiation decreases the uptake of iron by the bone marrow. In the present series of experiments the hyperferremia following acute whole-body irradiation (800 r) was found to reach its peak on the fourth day, at which time the iron-binding globulins were almost completely saturated. The radiation dose did not affect the iron-binding mechanism even when the globulins were saturated prior to irradiation because the saturation prolonged the period of hyperferremia. The results of this investigation support the theory that irradiation hyperferremia is a result of decreased iron utilization by the bone marrow. There does not appear to be any relationship between radiation lethality and hyperferremia.

Two figures.

Influence of Abdominal Radiation on Response of Rabbits to Intravenous Endotoxin. Bruce W. Jarvis, Wayne H. Schrader, and Joel G. Brunson. Arch. Path. **65:** 561–569, May 1958. (University of Minnesota Medical School, Minneapolis 14, Minn.)

Two hundred hybrid albino rabbits of both sexes, weighing 1 to 1.5 kg., were used in experiments to determine the influence of abdominal irradiation on response to intravenous endotoxin. Microscopic studies of the kidney, spleen, liver, heart, and lungs were made after irradiation with 300 r, 600 r, 1,200 r, and 2,400 r, in air, followed at various intervals by injection of a Gram-negative endotoxin.

Diffuse vascular fibrinoid lesions similar to those occurring in a generalized Shwartzman phenomenon were observed in all groups of animals but varied extensively in incidence. At each dose range of irradiation, the interval after which endotoxin was given appeared to alter the number of animals in which lesions developed. With 300 r in air, and with 2,400 r in air, an interval of eighteen hours between irradiation and endotoxin resulted in a greater number of lesions; with 600 r in air or 1,200 r in air, the optimal interval was twenty-four hours.

With dosages of 300 or 600 r in air followed by endotoxin, there were no acute deaths. However, when the animals were given endotoxin in conjunction with 1,200 r in air, 8 of 32 died within twelve hours after the administration of the toxin, and of 32 given 2,400 r in air, 5 died within a like period. In each group the greatest incidence of deaths occurred when the interval between irradiation and administration of endotoxin was twelve hours.

The data suggest that proper combinations of radiation and toxin may provide a method of producing controlled localized vascular fibrinoid lesions. The high incidence of diffuse lesions also suggests that, in addition to local effects, high quantities of abdominal irradiation may produce systemic vascular changes. Several possible mechanisms of action concerning the pathogenesis of the lesions are discussed.

Seven photomicrographs; 5 tables.

Stimulation of Feeler Reflexes in Snails by Roentgen and Alpha Rays. Otto D. Hug. Strahlentherapie **106**: 155–160, May 1958. (In German) (Biologische Institut der Phil.-Theol. Hochschule Regensburg, Germany)

The author examined ten varieties of ground and water snails in an attempt to determine the effect of ionizing radiation on the feeler reflexes. For his experiments he used x-rays (50 kv), beta rays from a strontium 90 source, and alpha rays from a polonium source.

All the animals responded similarly to the roentgen radiation, with a definite retraction of the feelers. The longest exposure was five minutes. If the body of the animal was covered with a layer of 3 mm. lead, the effect did not take place. The rate of irradiation varied from 1.5 to 15 r per second. From five to fifteen seconds were required to induce the reflex.

Beta rays were ineffective. Alpha rays, however, produced a good response. The polonium preparation was held at a distance of 3.9 cm. The reflex was observed with an exposure time of 0.02 seconds.

The author points out that the observation on snails is one of the most sensitive radiobiological tests. In an attempt to explain this reflex, he comes to the conclusion that ionizing rays must have an ability to act as stimuli to nerve endings. There may be some photo- or chemoreceptors present which are incited by the nerve impulse. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.